? ds

Set	Items	Description
S1	15749	TAU AND ALZHEIMER?
S2	102	S1 AND PROTEIN(W)SEQUENC?
S3	74	RD S2 (unique items)
S4	19	S3 AND PY<1992
S5	10505	TAU AND PHOSPHORYLAT?
S6	1397	S5 AND PY<1993
S7	602	RD S6 (unique items)
S8	302	S7 AND ALZHEIMER?
S9	95	S7 AND EPITOPE?
S10	0	S9 NOT S7
S11	10	S9 NOT S8

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---Logging off of Dialog---

? logoff

$%^Dialog;HighlightOn=%%%;HighlightOff=%%%;

Logging in to Dialog

Trying 3106900061...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
****
ENTER PASSWORD:
wolf
****
Welcome to DIALOG

Dialog leel 02.01.23D

Lat logoff: 29jan02 14:03:55
Logon file405 08feb02 13:43:46
*** ANNOUNCEMENT ***
***
--Connect Time join DialUnit a pricing
option on Dialog. See HELP CONNECT for
information.
***
--SorceOne patent are now deliered to or
email inbox a PDF replacing TIFF delier.
See HELP SOURCE1 for more information.
***
--Important new for pblic and academic
librarie. See HELP LIBRARY for more information.
***
--Important Notice to Freelance Athor--
See HELP FREELANCE for more information
***
NEW FILES RELEASED
***TEME - Technolog and Management(File 95)
***NewRx Weekl Report (File 135)
***TRADEMARKSCAN-Japan (File 669)
***Financial Time Fltext (File 476)
***
UPDATING RESUMED
***Delphe Eropean Bine (File 481)
***
RELOADED
***CLAIMS/US PATENTS (File 340, 341, 942)
***Kompa Middle Eat/Africa/Mediterranean (File 585)
***Kompa Aia/Pacific (File 592)
***Kompa Central/Eatern Erope (File 593)
***Kompa Canada (File 594)
***CANCERLIT (File 159)
***D&B - Dn' Market Identifier (516)
***Information Science Abtract (File 202)

REMOVED
***Tax Note Toda (File 790)
***State Tax Toda (File 791)
***Worldwide Tax Dail (File 792)
***Cort Filing (File 793)

New docment pplier
IMED ha been changed to INFOTRIE (ee HELP OINFOTRI)

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new erice. Firt Releae pdate major newwire
databae within 15 minte of tranmiion oer the
wire. Firt Releae proide fll Dialog earchabilit
and fll-text featre. To earch Firt Releae file in
OneSearch impl BEGIN FIRST for coerage from Dialog'
broad pectrm of new wire.

>>> Enter BEGIN HOMEBASE for Dialog Annoncement <<<
>>> of new databae, price change, etc. <<<
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**** ****
SYSTEM:HOME

Cot i in DialUnit
Men Stem II: D2 erion 1.7.8 term=ASCII
*** DIALOG HOMEBASE(SM) Main Men ***

Information:
1. Annoncement (new file, reload, etc.)
2. Databae, Rate, & Command Decription
3. Help in Chooing Databae for Yor Topic
4. Ctomer Serice (telephone aitance, training, eminar, etc.)
5. Prodct Decription

Connection:
6. DIALOG(R) Docment Delier
7. Data Star(R)

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/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option nmber to iew information or to connect to an online
erice. Enter a BEGIN command pl a file nmber to earch a databae
(e.g., B1 for ERIC).
? dialog

>>Invalid Option Number

*** DIALOG HOMEBASE(SM) Main Menu ***

Information:
1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:
6. DIALOG(R) Document Delivery
7. Data Star(R)

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/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online
service. Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? b 410

08feb02 13:43:48 User226352 Session D606.1
$0.00 0.229 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.00 Estimated cost this search
$0.00 Estimated total session cost 0.229 DialUnits

File 410:Chronolog(R) 1981-2002/Jan
(c) 2002 The Dialog Corporation

Set Items Description
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? set hi %%%;set hi %%%

HILIGHT set on as '%%%'%%%
%%%HILIGHT set on as '%%%'
? b biochem

08feb02 13:45:49 User226352 Session D606.2
$0.00 0.072 DialUnits File410
$0.00 Estimated cost File410
$0.20 TYMNET
$0.20 Estimated cost this search
$0.20 Estimated total session cost 0.301 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2002/Feb W1

FILE COPY

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      (c) 2002 BIOSIS
  File  6:NTIS 1964-2002/Feb W4
      (c) 2002 NTIS, Intl Cpyrght All Rights Res
*File  6: See HELP CODES6 for a short list of the Subject Heading Codes
(SC=, SH=) used in NTIS.
  File 34:SciSearch(R) Cited Ref Sci 1990-2002/Feb W2
      (c) 2002 Inst for Sci Info
  File 40:Enviroline(R) 1975-2002/Jan
  File 41:Pollution Abs 1970-2002/Jan
      (c) 2002 Cambridge Scientific Abstracts
  File 50:CAB Abstracts 1972-2002/Jan
      (c) 2002 CAB International
*File 50: Truncating CC codes is recommended for full retrieval.
See Help News50 for details.
  File 65:Inside Conferences 1993-2002/Feb W1
      (c) 2002 BLDSC all rts. reserv.
  File 68:Env.Bib. 1974-2002/Dec
      (c) 2002 Internl Academy at Santa Barbara
  File 71:ELSEVIER BIOBASE 1994-2002/Feb W1
      (c) 2002 Elsevier Science B.V.
  File 73:EMBASE 1974-2002/Feb W1
      (c) 2002 Elsevier Science B.V.
*File 73: For information about Explode feature please
see Help News73.
  File 76:Life Sciences Collection 1982-2002/Jan
      (c) 2002 Cambridge Sci Abs
*File 76: UDs have been manually adjusted to reflect the current months
data. There is no data missing.
  File 77:Conference Papers Index 1973-2002/Jan
      (c) 2002 Cambridge Sci Abs
  File 94:JICST-EPlus 1985-2002/Dec W5
      (c)2002 Japan Science and Tech Corp(JST)
*File 94: There is no data missing. UDs have been adjusted to reflect
the current months data. See Help News94 for details.
  File 98:General Sci Abs/Full-Text 1984-2001/Dec
      (c) 2002 The HW Wilson Co.
  File 103:Energy SciTec 1974-2001/Sep B2
      (c) 2001 Contains copyrighted material
*File 103: For updates please see Help News103.
For access restrictions, see HELP RESTRICT.
  File 143:Biol. & Agric. Index 1983-2001/Dec
      (c) 2002 The HW Wilson Co
  File 144:Pascal 1973-2002/Feb W1
      (c) 2002 INIST/CNRS
  File 155:MEDLINE(R) 1966-2002/Jan W2
  File 156:ToxFile 1966-2001/Oct W3
      (c) 2001
*File 156: File temporarily is not updating.  Updating expected to
resume in February 2002.
  File 162:CAB HEALTH 1983-2001/Dec
      (c) 2002 CAB INTERNATIONAL
*File 162: Truncating CC codes is recommended for full retrieval.
See Help News162 for details.
  File 172:EMBASE Alert 2002/Feb W1
      (c) 2002 Elsevier Science B.V.
  File 305:Analytical Abstracts 1980-2002/Feb W1
      (c) 2002 Royal Soc Chemistry
*File 305: Frequency of updates and Alerts changing to weekly.
See HELP NEWS 305.
  File 369:New Scientist 1994-2002/Jan W3
      (c) 2002 Reed Business Information Ltd.
  File 370:Science 1996-1999/Jul W3
      (c) 1999 AAAS
*File 370: This file is closed (no updates). Use File 47 for more current
information.
  File 399:CA SEARCH(R) 1967-2002/UD=13606
      (c) 2002 AMERICAN CHEMICAL SOCIETY
*File 399: Use is subject to the terms of your user/customer agreement.
RANK charge added; see HELP RATES 399.
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
      (c) 1998 Inst for Sci Info

    Set  Items  Description
    ---  -----  -----------
? s tau and Alzheimer?
      124140  TAU
      247636  ALZHEIMER?
   S1   15749  TAU AND ALZHEIMER?
? s s1 and protein(w)sequenc?

Processing
Processed 10 of 26 files ...
Processing
Processed 20 of 26 files ...
Completed processing all files
       15749  S1
     7340492  PROTEIN
     3457572  SEQUENC?
      227443  PROTEIN(W)SEQUENC?
   S2    102  S1 AND PROTEIN(W)SEQUENC?
? rd s2

...examined 50 records (50)
...examined 50 records (100)
...completed examining records
   S3     74  RD S2 (unique items)
? s s3 and PY<1992

Processing
Processed 10 of 26 files ...
>>>One or more prefixes are unsupported
>>> or undefined in one or more files.
Processing
Processing
Processed 20 of 26 files ...
Processing
Completed processing all files
         74  S3
   63063250  PY<1992
   S4    19  S3 AND PY<1992
? t s4


 4/2/1    (Item 1 from file: 5)
DIALOG(R)File  5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

07410662  BIOSIS NO.: 000040024971
%%%TAU%%% IN PHF
AUTHOR: MORI H; IHARA Y
AUTHOR ADDRESS: CENT. NEUROL. DISEASES, HARV. MED. SCH.,
BRIGHAM AND
 WOMEN'S HOSP., BOSTON, MASS. 02115, USA.
JOURNAL: MIYATAKE, T., D. J. SELKOE AND Y. IHARA (ED.).
INTERNATIONAL
CONGRESS SERIES, 884. MOLECULAR BIOLOGY AND GENETICS OF
ALZHEIMER'S
DISEASE; INTERNATIONAL SYMPOSIUM ON DEMENTIA, NIIGATA,
JAPAN, NOVEMBER
11-14, 1989. XV+288P. ELSEVIER SCIENCE PUBLISHERS B.V.
(BIOMEDICAL
DIVISION): AMSTERDAM, NETHERLANDS; (DIST. FOR THE USA AND
CANADA BY
ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK).
ILLUS. ISBN
0-444-81112-5. 0 (0). 1990. 29-36. %%%1990%%%
CODEN: EXMDA
RECORD TYPE: Citation
LANGUAGE: ENGLISH
DESCRIPTORS: HUMAN PAIRED HELICAL FILAMENTS
%%%ALZHEIMER%%%'S DISEASE
MOLECULAR SEQUENCE DATA %%%PROTEIN%%% %%%SEQUENCE%%%
CONCEPT CODES:
 07004  Behavioral Biology-Human Behavior
 10064  Biochemical Studies-Proteins, Peptides and Amino Acids
 20506  Nervous System-Pathology
 21002  Psychiatry-Psychopathology; Psychodynamics and Therapy
 00520  General Biology-Symposia, Transactions and Proceedings of
        Conferences, Congresses, Review Annuals
BIOSYSTEMATIC CODES:
 86215  Hominidae
```

BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA):
Animals
Chordates
Vertebrates
Mammals
Primates
Humans
? t s4/7/all

>>>Format 7 is not valid in file 143

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07410662 BIOSIS NO.: 000040024971
%%%TAU%%% IN PHF
AUTHOR: MORI H; IHARA Y
AUTHOR ADDRESS: CENT. NEUROL. DISEASES, HARV. MED. SCH., BRIGHAM AND
WOMEN'S HOSP., BOSTON, MASS. 02115, USA.
JOURNAL: MIYATAKE, T., D. J. SELKOE AND Y. IHARA (ED.). INTERNATIONAL
CONGRESS SERIES, 884. MOLECULAR BIOLOGY AND GENETICS OF ALZHEIMER'S
DISEASE; INTERNATIONAL SYMPOSIUM ON DEMENTIA, NIIGATA, JAPAN, NOVEMBER
11-14, 1989. XV+288P. ELSEVIER SCIENCE PUBLISHERS B.V. (BIOMEDICAL
DIVISION): AMSTERDAM, NETHERLANDS; (DIST. FOR THE USA AND CANADA BY
ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK). ILLUS. ISBN
0-444-81112-5. 0 (0). 1990. 29-36. %%%1990%%%
CODEN: EXMDA
RECORD TYPE: Citation
LANGUAGE: ENGLISH

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07410661 BIOSIS NO.: 000040024970
THE PHOSPHORYLATION SITE OF THE %%%TAU%%% IN PAIRED HELICAL FILAMENTS AN
IMMUNOCHEMICAL APPROACH
AUTHOR: IHARA Y; MIURA R; KONDO J; HAYASE T
AUTHOR ADDRESS: 2ND LAB. CLIN. PHYSIOL., TOKYO METROPOLITAN INST.
GERONTOL., ITABASHI-KU, TOKYO 173, JAPAN.
JOURNAL: MIYATAKE, T., D. J. SELKOE AND Y. IHARA (ED.). INTERNATIONAL
CONGRESS SERIES, 884. MOLECULAR BIOLOGY AND GENETICS OF ALZHEIMER'S
DISEASE; INTERNATIONAL SYMPOSIUM ON DEMENTIA, NIIGATA, JAPAN, NOVEMBER
11-14, 1989. XV+288P. ELSEVIER SCIENCE PUBLISHERS B.V. (BIOMEDICAL
DIVISION): AMSTERDAM, NETHERLANDS; (DIST. FOR THE USA AND CANADA BY
ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK). ILLUS. ISBN
0-444-81112-5. 0 (0). 1990. 21-28. %%%1990%%%
CODEN: EXMDA
RECORD TYPE: Citation
LANGUAGE: ENGLISH

4/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07375324 BIOSIS NO.: 000091002004
PHOSPHORYLATION OF MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% IDENTIFICATION
OF THE SITE FOR CALCIUM CALMODULIN DEPENDENT KINASE AND RELATIONSHIP WITH
%%%TAU%%% PHOSPHORYLATION IN %%%ALZHEIMER%%% TANGLES
AUTHOR: STEINER B; MANDELKOW E-M; BIERNAT J; GUSTKE N; MEYER H E; SCHMIDT B
; MIESKES G; SOELING H D; DRECHSEL D; ET AL
AUTHOR ADDRESS: INQ. E. MANDEKOW, MAX-PLANCK-UNIT STRUCTURAL MOL. BIOL.,
C/O DESY, NOTKESTRASSE 85, D-2000 HAMBURG 52, W. GER.
JOURNAL: EMBO (EUR MOL BIOL ORGAN) J 9 (11). 1990. 3539-3544. %%%1990%%%
FULL JOURNAL NAME: EMBO (European Molecular Biology Organization) Journal
CODEN: EMJOD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The microtubule array in neuronal cells undergoes extensive growth, dynamics and rearrangements during neurite outgrowth. While little is known about how these changes are regulated, microtuble-associated proteins (MAPs) including %%%tau%%% protein are likely to perform an important role. %%%Tau%%% is one of the MAPs in mammalian brain. When isolated it is usually a mixture of several isoforms containing between 341 and 441 residues that arise from alternative splicing. %%%Tau%%% can be phosphorylated by several protein
kinases. Phosphorylation at certain sites results in major structural and functional changes, as seen by changes in electrophoretic mobility, interaction with microtubules, molecular length and elasticity. Here we show that the sites of phosphorylation by four kinases (PKA, PKC, CK and CaMK) all lie in the C-terminal microtubule-binding half of %%%tau%%%, but only the phosphorylation by CaM kinase shows the pronounced shift in electrophoretic mobility characteristic for %%%tau%%% from %%%Alzheimer%%% neurofibrillary tangels. By using a combination of limited proteolysis, %%%protein%%% %%%sequencing%%% and protein engineering we show that a single phosphorylation site is responsible for this shift, located at Ser 405 in the C-terminal tail of the protein outside the region of internal repeats. Phosphorylation at this site not only reduces the electrophoretic mobility of %%%tau%%%, it also makes the
protein long and stiff, as shown earlier. The site is likely to be phosphorylated in %%%tau%%% from %%%Alzheimer%%% neurofibrillary tangles.

4/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06743025 BIOSIS NO.: 000088052455
BIOCHEMISTRY OF PAIRED HELICAL FILAMENTS PHF
AUTHOR: IHARA Y
AUTHOR ADDRESS: TOKYO METROPOLITAN INST. GERONTOL., JPN.
JOURNAL: JPN J GERIATR 25 (4). 1988. 364-367. %%%1988%%%
FULL JOURNAL NAME: Japanese Journal of Geriatrics
CODEN: NIRZA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Since 1980, the nature of PHF has been heavily focused in several
laboratories. The most unexpected observation was that PHF are insoluble in harsh denaturants or detergents including SDS, urea and guanidine HCl. This unusual insolubility of PHF made possible high grade purification of PHF, but prevented the application of analytical biochemical methods to the identification of the PHF components. Therefore, we took an immunochemical approach using specific antibodies to PHF, which were prepared by immunization of purified PHF. Our strategy was to search for soluble polypeptides reactive with antiPHF, instead of analyzing PHF directly. Polyclonal antibodies to PHF were found to label %%%tau%%%, a neuron-specific microtubule-associated phosphoprotein. The analysis of PHF antisera showed that there are two populations of %%%tau%%% antibodies; one is reactive with both phosphorylated and nonphosphorylated forms of %%%tau%%%, the other is specific for phosphorylated %%%tau%%%. In addition, antibodies specific for nonphosphorylated %%%tau%%% could not be detected in the PHF antisera.
From these observations, one of the antigenic determinants of PHF has been considered as phosphorylated %%%tau%%%. A hybridoma producing a monoclonal antibody to PHF (DF2) was obtained by the fusion of mouse myeloma cells and rat spleen cells immunized with PHF. DF2 was confirmed to specifically bind to PHF. In the blot of the soluble fraction of brain homogenates, DF2 labeled a small polypeptide Mr .apprx. 5 kD, which was identified as ubiquitin by its purification and subsequent %%%protein%%% %%%sequencing%%%. Moreover, five ubiquitin fragments were identified in the PHF digest. Thus ubiquitin is a component of PHF. Two components, %%%tau%%% and ubiquitin, have been identified in PHF immunochemically and
protein chemically, respectively. Two lines of evidence suggest that PHF contain the components other than %%%tau%%% or ubiquitin: first, ghost tangles (extracellular tangles) are not stained with antiPHF or %%%tau%%%
antibodies, although they appear to be made of PHF. Second, the staining activity of antiPHF cannot be absorbed out with excess amount of %%%tau%%%. These strongly suggest that PHF contain as-yet-unidentified components.

4/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06380131 BIOSIS NO.: 000036083284
EPITOPES THAT SPAN THE %%%TAU%%% MOLECULAR ARE SHARED WITH PAIRED HELICAL
FILAMENTS
AUTHOR: KOSIK K S; ORECCHIO L D; BINDER L; TROJANOWSKI J Q; LEE V M-Y; LEE
G
AUTHOR ADDRESS: HARVARD MED. SCH., BOSTON, MA.
JOURNAL: JOINT MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY AND THE
AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, SAN FRANCISCO,
CALIFORNIA, USA, JANUARY 29-FEBRUARY 2, 1989. J CELL BIOL 107 (6 PART 3).
1988. 461A. %%%1988%%%
CODEN: JCLBA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

4/7/6 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00755545 Genuine Article#: EU497 Number of References: 33
Title: THE ENDOPLASMIC-RETICULUM RETENTION SIGNAL OF THE E3/19K PROTEIN OF
ADENOVIRUS-2 IS MICROTUBULE BINDING
Author(s): DAHLLOF B; WALLIN M; KVIST S
Corporate Source: LUDWIG INST CANC RES,STOCKHOLM BRANCH,BOX 60202/S-10401
STOCKHOLM//SWEDEN/; LUDWIG INST CANC RES,STOCKHOLM BRANCH,BOX
60202/S-10401 STOCKHOLM//SWEDEN/; GOTHENBURG UNIV,DEPT ZOOPHYSIOL/S-40031 GOTHENBURG//SWEDEN/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, %%%1991%%%, V266, N3, P1804-1808
Language: ENGLISH Document Type: ARTICLE

4/7/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

04455185 EMBASE No: 1990343294
Phosphorylation of microtubule-associated protein %%%tau%%%: Identification of the site for Casup 2sup +-calmodulin dependent kinase and relationship with %%%tau%%% phosphorylation in %%%Alzheimer%%% tangles
Steiner B.; Mandelkow E.-M.; Biernat J.; Gustke N.; Meyer H.E.; Schmidt B.; Mieskes G.; Soling H.D.; Drechsel D.; Kirschner M.W.; Goedert M.; Mandelkow E.
Max-Planck-Unit for, Structural Molecular Biology, c/o DESY, Notkestrasse
85,D-2000 Hamburg 52 Germany
EMBO Journal (EMBO J.) (United Kingdom) 1990, 9/11 (3539-3544)
CODEN: EMJOD ISSN: 0261-4189
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The microtubule array in neuronal cells undergoes extensive growth, dynamics and rearrangements during neurite outgrowth. While little is known about how these changes are regulated, microtubule-associated proteins (MAPs) including %%%tau%%% protein are likely to perform an important role.
%%%Tau%%% is one of the MAPs in mammalian brain. When isolated it is usually a mixture of several isoforms containing between 341 and 441 residues that arise from alternative splicing. %%%Tau%%% can be phosphorylated by several protein kinases. Phosphorylation at certain sites results in major structural and functional changes, as seen by changes in electrophoretic mobility, interaction with microtubules, molecular length and elasticity. Here we show that the sites of phosphorylation by four kinases (PKA, PKC, CK and CaMK) all lie in the C-terminal microtubule-binding half of %%%tau%%%, but only the phosphorylation by CaM
kinase shows the pronounced shift in electrophoretic mobility characteristic for %%%tau%%% from %%%Alzheimer%%% neurofibrillary tangles.
By using a combination of limited proteolysis, %%%protein%%% %%%sequencing%%% and protein engineering we show that a single phosphorylation site is responsible for this shift, located at Ser 405 in the C-terminal tail of the protein outside the region of internal repeats. Phosphorylation at this site not only reduces the electrophoretic mobility of %%%tau%%%, it also makes the protein long and stiff, as shown earlier. The site is likely to be phosphorylated in %%%tau%%% from %%%Alzheimer%%%
neurofibrillary tangles.

4/7/8 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06962794 91006052 PMID: 2120043
Phosphorylation of microtubule-associated protein %%%tau%%% : identification of the site for Ca2(+)-calmodulin dependent kinase and relationship with %%%tau%%% phosphorylation in %%%Alzheimer%%% tangles.
Steiner B; Mandelkow EM; Biernat J; Gustke N; Meyer HE; Schmidt B; Mieskes G; Soling HD; Drechsel D; Kirschner MW; et al
Max-Planck-Unit for Structural Molecular Biology, Hamburg, FRG.
EMBO journal (ENGLAND) Nov %%%1990%%%, 9 (11) p3539-44, ISSN
0261-4189 Journal Code: EMB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The microtubule array in neuronal cells undergoes extensive growth, dynamics and rearrangements during neurite outgrowth. While little is known about how these changes are regulated, microtubule-associated proteins (MAPs) including %%%tau%%% protein are likely to perform an important role.
%%%Tau%%% is one of the MAPs in mammalian brain. When isolated it is
usually a mixture of several isoforms containing between 341 and 441 residues that arise from alternative splicing. %%%Tau%%% can be phosphorylated by several protein kinases. Phosphorylation at certain sites results in major structural and functional changes, as seen by changes in electrophoretic mobility, interaction with microtubules, molecular length and elasticity. Here we show that the sites of phosphorylation by four kinases (PKA, PKC, CK and CaMK) all lie in the C-terminal microtubule-binding half of %%%tau%%%, but only the phosphorylation by CaM
kinase shows the pronounced shift in electrophoretic mobility characteristic for %%%tau%%% from %%%Alzheimer%%% neurofibrillary tangles.
By using a combination of limited proteolysis, %%%protein%%% %%%sequencing%%% and protein engineering we show that a single phosphorylation site is responsible for this shift, located at Ser 405 in the C-terminal tail of the protein outside the region of internal repeats. Phosphorylation at this site not only reduces the electrophoretic mobility of %%%tau%%%, it also makes the protein long and stiff, as shown earlier. The site is likely to be phosphorylated in %%%tau%%% from %%%Alzheimer%%%
neurofibrillary tangles.

4/7/9 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05969558 90166561 PMID: 2483105
The carboxyl third of %%%tau%%% is tightly bound to paired helical filaments.
Kondo J; Honda T; Mori H; Hamada Y; Miura R; Ogawara M; Ihara Y
Mitsubishi Kasei Corporation Research Center, Biosciences Laboratory, Yokohama, Japan.
Neuron (UNITED STATES) Nov %%%1988%%%, 1 (9) p827-34, ISSN
0896-6273 Journal Code: AN8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
To obtain definitive evidence that %%%tau%%% is a component of paired
helical filaments (PHF) in %%%Alzheimer%%%'s disease, we fractionated and
sequenced PHF-derived peptides according to a previously described procedure. In the PHF digest, we found four independent %%%tau%%% peptides
that were located in the carboxyl third of %%%tau%%%. Subsequent extensive
analysis of the PHF digest did not provide any other %%%tau%%% peptides.
The conventional PHF antiserum and a new antiserum directed toward formic
acid-denatured PHF reacted with the distinct CNBr fragments of %%%tau%%%
localized on the carboxy-terminal portion of %%%tau%%% by %%%protein%%%
%%%sequencing%%%. From these observations, we conclude that the carboxyl
third of %%%tau%%% is tightly bound to PHF.
Record Date Created: 19900406

4/7/10 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

116039053 CA: 116(5)39053h JOURNAL
Multiple isoforms of human microtubule-associated protein tau: sequences and localization in neurofibrillary tangles of Alzheimer's disease
AUTHOR(S): Goedert, M.; Spillantini, M. G.; Jakes, R.; Rutherford, D.; Crowther, R. A.
LOCATION: Lab. Mol. Biol., Med. Res. Counc., Cambridge, UK, CB2 2QH
JOURNAL: Neuron DATE: 1989 VOLUME: 3 NUMBER: 4 PAGES: 519-26 CODEN:
NERNET ISSN: 0896-6273 LANGUAGE: English
SECTION:
CA214010 Mammalian Pathological Biochemistry
CA203XXX Biochemical Genetics
IDENTIFIERS: tau protein isoform sequence Alzheimer disease, gene tau

protein isoform sequence Alzheimer
DESCRIPTORS:
Gene,animal...
for tau protein isoforms of humans, sequence and developmental and Alzheimer's disease-related expression of
Tau factors...
isoforms of, of brain of humans, sequence and developmental and Alzheimer's disease-related expression of
Protein sequences...
of tau protein isoforms of brain of human, complete
Deoxyribonucleic acid sequences...
tau factor-specifying, isoforms of, of brain of human, complete
Ribonucleic acids,messenger...
tau factor-specifying, isoforms of, of brain of humans, age and Alzheimer's disease effect on
Mental disorder,Alzheimer's disease...
tau protein isoforms expression in neurofibrillary tangles of brain in, of humans
Brain,composition...
tau protein isoforms of, age and Alzheimer's disease effect on, of humans
Embryo,fetus...
tau protein isoforms of brain of human
CAS REGISTRY NUMBERS:
138237-56-6 138237-57-7 138237-58-8 138237-59-9 amino acid sequence of
138237-60-2 138237-61-3 138237-62-4 nucleotide sequence of

4/7/11 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

115253252 CA: 115(23)253252v JOURNAL
Identification of 3- and 4-repeat tau isoforms within the PHF in Alzheimer's disease
AUTHOR(S): Jakes, Ross; Novak, Michal; Davison, Matthew; Wischik, Claude
M.
LOCATION: Lab. Mol. Biol., MRC Cent., Cambridge, UK, CB2 2QH
JOURNAL: EMBO J. DATE: 1991 VOLUME: 10 NUMBER: 10 PAGES: 2725-9
CODEN: EMJODG ISSN: 0261-4189 LANGUAGE: English
SECTION:
CA214010 Mammalian Pathological Biochemistry
CA203XXX Biochemical Genetics
IDENTIFIERS: tau factor paired helical filament Alzheimer
DESCRIPTORS:
Tau factors...
isoforms, of pronase-resistant paired helical filament core, of brain, in Alzheimer's disease of humans, characterization of
Protein sequences...
of tau protein isoforms, of paired helical filament cores, of brain, in Alzheimer's disease of humans
Mental disorder,Alzheimer's disease...
pathogenesis of, tau protein isoforms of brain paired helical filaments characterization in relation to, of humans
Proteins,specific or class, paired helical filament core...
tau isoforms, of brain, in Alzheimer's disease of humans, characterization of
Brain,composition...
tau protein isoforms of paired helical filaments of, in Alzheimer's disease of humans, characterization of
Organelle,paired helical filament...
tau protein isoforms of pronase-resistant core of, of brain, in Alzheimer's disease of humans, characterization of
CAS REGISTRY NUMBERS:
137261-10-0 amino acid sequence of

4/7/12 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

115205044 CA: 115(19)205044g JOURNAL
Difference between the tau protein of Alzheimer paired helical filament core and normal tau revealed by epitope analysis of monoclonal antibodies 423 and 7.51
AUTHOR(S): Novak, Michal; Jakes, Ross; Edwards, Patricia C.; Milstein, Cesar; Wischik, Claude M.
LOCATION: Lab. Mol. Biol., Med. Res. Counc., Cambridge, UK, CB2 2QH
JOURNAL: Proc. Natl. Acad. Sci. U. S. A. DATE: 1991 VOLUME: 88
NUMBER: 13 PAGES: 5837-41 CODEN: PNASA6 ISSN: 0027-8424
LANGUAGE:
English
SECTION:
CA214010 Mammalian Pathological Biochemistry
CA206XXX General Biochemistry
IDENTIFIERS: tau protein paired helical filament Alzheimer
DESCRIPTORS:
Proteins,specific or class, paired helical filament core...
human tau factor epitopes as defined by monoclonal antibodies in relation to
Organelle,paired helical filament...
in Alzheimer's disease, human tau factor epitope defined by monoclonal antibodies in relation to
Tau factors...
monoclonal antibody-defined epitope of human, paired helical filament core in Alzheimer's disease in relation to
Protein sequences...
of tau factor, of human
Mental disorder,Alzheimer's disease...
paired helical filament formation in, human tau factor epitopes as defined by monoclonal antibodies in relation to
Antibodies,monoclonal...
tau factor epitopes defined by, paired helical filament core in Alzheimer's disease in relation to, human
CAS REGISTRY NUMBERS:
136857-47-1 amino acid sequence of

4/7/13 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

113228849 CA: 113(25)228849w JOURNAL
Alz-50 recognizes a phosphorylated epitope of tau protein
AUTHOR(S): Ueda, K.; Masliah, E.; Saitoh, T.; Bakalis, S. L.; Scoble, H.; Kosik, K. S.
LOCATION: Sch. Med., Univ. California, San Diego, La Jolla, CA, 92093, USA
JOURNAL: J. Neurosci. DATE: 1990 VOLUME: 10 NUMBER: 10 PAGES: 3295-304 CODEN: JNRSDS ISSN: 0270-6474 LANGUAGE: English
SECTION:
CA214010 Mammalian Pathological Biochemistry
IDENTIFIERS: tau phosphoprotein Alzheimer brain helical filament, monoclonal antibody tau protein brain Alzheimer
DESCRIPTORS:
Antibodies,monoclonal...
Alz-50, to .tau. phosphoprotein carboxy terminal region, of brain paired helical filaments, in Alzheimer's disease of humans
Tau factors...
amino acid sequence of carboxy terminal region of, of brain paired helical filaments, in Alzheimer's disease of humans
Protein sequences...
of .tau. phosphoprotein carboxy terminal region, of brain paired helical filaments, in Alzheimer's disease of humans
Mental disorder,Alzheimer's disease...
.tau. phosphoprotein of brain paired helical filaments in, monoclonal antibody in study of, of humans
Brain,cerebrum,composition...
.tau. phosphoprotein of paired helical filaments in, monoclonal antibody in study of, in Alzheimer's disease of humans
Organelle,paired helical filament...
.tau. phosphoprotien of, of brain, monoclonal antibody in study of, in Alzheimer's disease of humans

4/7/14 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

111209928 CA: 111(23)209928p JOURNAL
Cloning and sequencing of the cDNA encoding an isoform of microtubule-associated protein tau containing four tandem repeats: differential expression of tau protein mRNAs in human brain
AUTHOR(S): Goedert, M.; Spillantini, M. G.; Potier, M. C.; Ulrich, J.; Crowther, R. A.
LOCATION: Lab. Mol. Biol., MRC, Cambridge, UK, CB2 2QH
JOURNAL: EMBO J. DATE: 1989 VOLUME: 8 NUMBER: 2 PAGES: 393-9 CODEN:
EMJODG ISSN: 0261-4189 LANGUAGE: English
SECTION:
CA203003 Biochemical Genetics
CA213XXX Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: protein tau isoform gene sequence human
DESCRIPTORS:
Gene and Genetic element,animal...
for tau protein isoform, of human, structure and stage- and tissue-specific expression of
Ribonucleic acids,messenger, tau factor-specifying...
isoforms of, of human, stage- and tissue-specific expression of
Deoxyribonucleic acid sequences,tau factor-specifying...
of human, complete
Protein sequences...
of tau protein, of human, complete
Tau factors...
sequences and stage- and tissue-specific expression of
Brain,neurofibrillary tangle,composition...
tau protein isoforms in, human Alzheimer's disease in relation to
Embryo...
tau protein mRNAs differential expression in, of human
Brain,metabolism...
tau protein mRNAs differential expression in, of human embryo
CAS REGISTRY NUMBERS:
123514-64-7 amino acid sequence of
123513-40-6 nucleotide sequence of

4/7/15 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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110210264 CA: 110(23)210264e JOURNAL
A distinct form of tau is selectively incorporated into Alzheimer's paired helical filaments
AUTHOR(S): Mori, Hiroshi; Hamada, Yoshio; Kawaguchi, Masahiro; Honda, Toshiyuki; Kondo, Jun; Ihara, Yasuo
LOCATION: 2nd Lab. Clin. Physiol., Tokyo Metrop. Inst. Gerontol., Tokyo, Japan, 173
JOURNAL: Biochem. Biophys. Res. Commun. DATE: 1989 VOLUME: 159 NUMBER: 3 PAGES: 1221-6 CODEN: BBRCA9 ISSN: 0006-291X LANGUAGE:
English
SECTION:
CA214010 Mammalian Pathological Biochemistry
CA203XXX Biochemical Genetics
CA213XXX Mammalian Biochemistry
IDENTIFIERS: tau isoform Alzheimer paired helical filament, brain aging tau isoform, mol cloning tau isoform
DESCRIPTORS:
Tau factors,3-repeat-type...
of Alzheimer's disease-assocd. paired helical filaments, of human
Tau factors,4-repeat-type...
of brain, in aging in human
Deoxyribonucleic acid sequences,4-repeat type tau factor-specifying...
of human
Protein sequences...
of tau factor isoforms, of human
Molecular cloning...
of 4-repeat type tau factor cDNA of human
Organelle,paired helical filament...
tau 3-repeat type of, in Alzheimer's disease in humans
Mental disorder,Alzheimer's disease...
tau 3-repeat type of paired helical filaments in, in humans
Senescence...
tau 4-repeat type of brain in, in humans
Brain,composition...
tau 4-repeat type of, in senescence in humans

4/7/16 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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110187175 CA: 110(21)187175r JOURNAL
Structure of the bovine Tau gene: alternatively spliced transcripts generate a protein family
AUTHOR(S): Himmler, Adolf
LOCATION: Genentech, Inc., South San Francisco, CA, 94080, USA
JOURNAL: Mol. Cell. Biol. DATE: 1989 VOLUME: 9 NUMBER: 4 PAGES: 1389-96 CODEN: MCEBD4 ISSN: 0270-7306 LANGUAGE: English
SECTION:
CA203003 Biochemical Genetics
CA206XXX General Biochemistry
CA213XXX Mammalian Biochemistry
IDENTIFIERS: bovine microtubule assocd protein Tau gene, Tau gene family
isoform transcript splicing
DESCRIPTORS:
Ribonucleic acid formation,messenger, tau factor-specifying...
alternative splicing in, in cow
Deoxyribonucleic acid sequences,tau factor-specifying...
exon-intron junctions and exon 14, of cow
Gene and Genetic element,animal...
for Tau protein isoforms, of cow, structure of and alternative splicing of mRNA of
Tau factors...
isoforms, of cow, alternative mRNA splicing in formation of
Protein sequences...
of Tau protein gene exon 14 product, of cow
Molecular cloning...
of Tau protein gene, of cow, in Escherichia coli
Cattle...
Tau protein gene of, alternative splicing of mRNA from, protein isoforms in relation to
Mental disorder,Alzheimer's disease...
Tau protein isoforms in, in human brain
Brain,composition...
Tau protein isoforms of, of cow, alternative mRNA splicing in formation of

4/7/17 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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110001922 CA: 110(1)1922d JOURNAL
Cloning and sequencing of the cDNA encoding a core protein of the paired helical filament of Alzheimer disease: identification as the microtubule-associated protein tau
AUTHOR(S): Goedert, M.; Wischik, C. M.; Crowther, R. A.; Walker, J. E.; Klug, A.
LOCATION: Med. Res. Counc. Lab. Mol. Biol., Cambridge, UK, CB2 2QH
JOURNAL: Proc. Natl. Acad. Sci. U. S. A. DATE: 1988 VOLUME: 85 NUMBER: 11 PAGES: 4051-5 CODEN: PNASA6 ISSN: 0027-8424 LANGUAGE:
English
SECTION:
CA203003 Biochemical Genetics
CA213XXX Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: Alzheimer brain protein tau cDNA sequence, mRNA protein tau
Alzheimer human brain, gene cloning human brain protein tau
DESCRIPTORS:
Ribonucleic acids,messenger, tau factor-specifying...
distribution of, in brain of human with Alzheimer disease
Gene and Genetic element,animal...
for protein tau, of human with Alzheimer disease, cloning and sequencing of
Deoxyribonucleic acid sequences,tau factor-specifying...
of brain of human with Alzheimer disease, complete

Tau factors... Transferrins,.tau.-...
of brain of human with Alzheimer disease, gene for, nucleotide and encoded peptide sequences of
Molecular cloning...
of protein tau gene, of human with Alzheimer disease
Protein sequences...
of protein tau, of brain of human with Alzheimer disease, complete
Microtubule...
protein tau assocd. with, of human with Alzheimer disease, cloning and sequencing of gene for
Mental disorder,Alzheimer's disease...
protein tau in, cloning and sequencing of gene for
Organelle,paired helical filament...
protein tau in, of human with Alzheimer disease, cloning and sequencing of gene for
Brain,composition...
tau protein in, of human with Alzheimer disease, cloning and sequencing of gene for
CAS REGISTRY NUMBERS:
117987-94-7 amino acid sequence of
117988-39-3 nucleotide sequence of

4/7/18 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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109071481 CA: 109(9)71481n JOURNAL
Isolation of a fragment of tau derived from the core of the paired helical filament of Alzheimer disease
AUTHOR(S): Wischik, C. M.; Novak, M.; Thoegersen, H. C.; Edwards, P. C.; Runswick, M. J.; Jakes, R.; Walker, J. E.; Milstein, C.; Roth, M.; Klug, A.
LOCATION: Med. Res. Counc. Lab. Mol. Biol., Cambridge, UK, CB2 2QH
JOURNAL: Proc. Natl. Acad. Sci. U. S. A. DATE: 1988 VOLUME: 85
NUMBER: 12 PAGES: 4506-10 CODEN: PNASA6 ISSN: 0027-8424
LANGUAGE:
English
SECTION:
CA214010 Mammalian Pathological Biochemistry
IDENTIFIERS: tau fragment paired helical filament Alzheimer
DESCRIPTORS:
Tau factors...
fragments, of paired helical filament cores in Alzheimers disease in humans
Protein sequences...
of tau fragments of paired helical filament cores in Alzheimers disease in humans
Mental disorder,Alzheimer's disease...
tau fragments from paired helical filament cores in, in humans
Organelle,paired helical filament...
tau fragments of core of, in Alzheimers disease in humans

4/7/19 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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109050389 CA: 109(7)50389y JOURNAL
Identification of the major multiphosphorylation site in mammalian neurofilaments
AUTHOR(S): Lee, Virginia M. Y.; Otvos, Laszlo, Jr.; Carden, Martin J.; Hollosi, Miklos; Dietzschold, Bernhard; Lazzarini, Robert A.
LOCATION: Sch. Med., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
JOURNAL: Proc. Natl. Acad. Sci. U. S. A. DATE: 1988 VOLUME: 85
NUMBER: 6 PAGES: 1998-2002 CODEN: PNASA6 ISSN: 0027-8424
LANGUAGE:
English
SECTION:
CA206003 General Biochemistry
IDENTIFIERS: phosphorylation site neurofilament protein mammal, evolution
phosphorylation site neurofilament protein
DESCRIPTORS:
Phosphoproteins,NF-H (neurofilament triplet, high-mol.-wt.)...
Phosphoproteins,NF-M (neurofilament triplet, medium-mol.-wt.)...
multiphosphorylation sites of, of human and other animals, identification and conservative evolution of
Mental disorder,Alzheimer's disease...
neurofibrillary tangles in, abnormal phosphorylation site of
Amphibian... Annelid... Bird... Fish... Mollusk...
neurofilament triplet proteins of, conservative evolution of phosphorylation site of
Mammal...
neurofilament triplet proteins of, multiphosphorylation site in
Phosphoproteins,microtubule-assocd., 2... Tau factors...
neurofilament triplets protein multiphosphorylation site antibody to mammal interaction with
Conformation and Conformers...
of neurofilament triplet protein multiphosphorylation sites, of mammals
Protein sequences...
of neurofilament triplet proteins multiphosphorylation site, of human and other animals
Phosphorylation,biological...
of neurofilament triplet proteins, of human and other animals, identification and conservative evolution of sites of
Evolution,conservative...
on neurofilament triplet protein multiphosphorylation sites
Cytoskeleton,neurofilament...
proteins of, multiphosphorylation site of, of human and other animals, sequence and conservative evolution of
CAS REGISTRY NUMBERS:
115397-57-4P 115470-46-7P prepn. and phosphorylation of
? ds

Set Items Description
S1 15749 TAU AND ALZHEIMER?
S2 102 S1 AND PROTEIN(W)SEQUENC?
S3 74 RD S2 (unique items)
S4 19 S3 AND PY<1992
? s tau and phosphorylat?

124140 TAU
661402 PHOSPHORYLAT?
S5 10505 TAU AND PHOSPHORYLAT?
? s s5 and py<1993

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>>> or undefined in one or more files.
Processing
Processed 20 of 26 files ...
Processing
Completed processing all files
10505 S5
67287585 PY<1993
S6 1397 S5 AND PY<1993
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...examined 50 records (150)
...examined 50 records (200)
...examined 50 records (250)
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...examined 50 records (400)
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...examined 50 records (1150)
...examined 50 records (1200)
...examined 50 records (1250)
...examined 50 records (1300)
...examined 50 records (1350)
...completed examining records
S7 602 RD S6 (unique items)
? t s7/7/1-5

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7/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08798405 BIOSIS NO.: 199395087756
The antineoplastic agent estramustine and the derivative estramustine phosphate inhibit secretion of interleukin-3 in leukemic cells: Possible roles of MAPs.
AUTHOR: Martinez Jorge(a); Santibanez Juan Francisco; Vial Clarisa; Maccioni Ricardo B
AUTHOR ADDRESS: (a)Inst. Nutricion y Tecnol. de Alimentos, Univ. de Chile, Casilla 138-11, Santiago**Chile
JOURNAL: Molecular and Cellular Biochemistry 117 (2):p165-173 %%%1992%%%
ISSN: 0300-8177
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The antineoplasic drug estramustine is an adduct of estradiol and nor-nitrogen mustard. It has been shown that this drug interferes with microtubule assembly, an effect mediated by estramustine interaction with microtubule-associated proteins (MAPs). In the present report we demonstrate that estramustine and the %%%phosphorylated%%% derivative of the drug, estramustine-phosphate, inhibit the secretion of interleukin-3 by WEHI-3B cells. These studies also show that the estramustine derivative specifically interacts with a MAPs component found in these cells, which exhibited characteristics resembling those of %%%tau%%% protein isoforms. Western blots using a unique monoclonal antibody MTB6.22 that recognizes microtubule-binding domains on MAPs, indicated that this WEHI protein factor contained the antigenic determinant that are functionally significant for microtubule assembly. ELISA assays using this antibody, also showed a decrease in the levels of the immunoreactive protein in WEHI cells after treatment with EMP. Interestingly, it has been recently described that the action of estramustine-phosphate is mediated by a direct interaction with MAP-binding sites on the microtubule surface, which are recognized by the site-specific monoclonal antibody. These findings together with immuno-precipitation experiments using anti-interleukin-3 antibodies and the inhibitory effect of the estramustine derivative on WEHI secretion process suggest that this anti-mitotic agent may block IL-3 secretion by a mechanism involving its interaction with a '%%%tau%%%-like' MAPs component present in these cells.

7/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08787957 BIOSIS NO.: 199395077308
Characterization of a neurofilament-associated kinase that %%%phosphorylates%%% the middle molecular mass component of chicken neurofilaments.
AUTHOR: Hollander Brian A; Bennett Gudrun S(a)
AUTHOR ADDRESS: (a)Dep. Anat. and Cell Biol., Box 100235, Health Sci. Cent., Univ. Fla. Coll. Med., Gainesville, FL**USA
JOURNAL: Brain Research 599 (2):p237-245 %%%1992%%%
ISSN: 0006-8993
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have examined the properties of a chicken neurofilament (NF) kinase partially purified from NF-enriched preparations. This kinase cosediments with NFs following extraction with Triton X-100 and can be separated in an active form from NFs by treatment with 0.8 M KCl. Sequential chromatography of the salt extract on DEAE-cellulose and phosphocellulose results in an approximately 500-fold increase in specific activity over endogenous NF preparations as measured by 32P-incorporation into the middle molecular mass component of NFs (NF-M). The kinase is Mg-2+-dependent, second messenger-independent and inhibited by high concentrations of heparin. It shows selectivity for NF-M and evidence is presented that the kinase %%%phosphorylates%%% NF-M solely in the tail domain. The kinase can also %%%phosphorylate%%% the microtubule-associated proteins %%%tau%%% and MAP2 as well as mammalian NF-M, all of which share putative %%%phosphorylation%%% sequences with chicken NF-M.

7/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08787925 BIOSIS NO.: 199395077276
%%%Phosphorylation%%% sites on %%%tau%%% by %%%tau%%% protein kinase I, a bovine derived kinase generating an epitope of paired helical filaments.
AUTHOR: Ishiguro Koichi(a); Omori Akira; Takamatsu Masako; Sato Kazuki; Arioka Manabu; Uchida Tsuneko; Imahori Kazutomo
AUTHOR ADDRESS: (a)Mitsubishi Kasei Inst. Life Sci., 11 Minamiooya, Machida-shi, Tokyo, 194**Japan
JOURNAL: Neuroscience Letters 148 (1-2):p202-206 %%%1992%%%
ISSN: 0304-3940
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Tau%%% protein kinase I (TPKI) isolated from bovine brain has been determined to phosphorylte %%%tau%%% at four distinct sites by detecting modified Ser and Thr residues with protein sequencer. Ser199, Thr231, Ser396 and Ser413 were all found to have been %%%phosphorylated%%% by TPKI (numbering of amino acids was done in relation to the longest human %%%tau%%% (Neuron, 3 (1989) 519-526)). These phophorylations generate an epitope of PHF (paired helical filaments) and eliminate the recognition of %%%tau%%% by the monoclonal antibody, %%%tau%%%-1. These results suggested that TPKI might be reponsible for at least some of the %%%phosphorylation%%% of %%%tau%%% to induce PHF formation

7/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08775405 BIOSIS NO.: 199395064756
Glycogen synthase kinase-3 induces Alzheimer's disease-like %%%phosphorylation%%% of %%%tau%%%: Generation of paired helical filament epitopes and neuronal localisation of the kinase.
AUTHOR: Hanger Diane P(a); Hughes Kenneth; Woodgett James R; Brion Jean-Pierre; Anderton Brian H
AUTHOR ADDRESS: (a)Dep. Neurosci., Inst. Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF**UK
JOURNAL: Neuroscience Letters 147 (1):p58-62 %%%1992%%%
ISSN: 0304-3940
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Glycogen synthase kinase-3 (GSK-3) reduced the mobility of

human
%%%tau%%% on SDS-PAGE, prevented binding of the monoclonal antibody (mAb), %%%Tau%%%.1, and induced binding of the mAb 8D8. Recombinant %%%tau%%% %%%phosphorylated%%% by GSK-3 aligned on SDS-PAGE with the
abnormally %%%phosphorylated%%% %%%tau%%% (PHF-%%%tau%%%) associated with
the paired helical filaments in Alzheimer's disease brain.
%%%Phosphorylated%%% serine-396 (numbering of the largest human brain
%%%tau%%% isoform) was identified as a binding site on %%%tau%%% for mAb
8D8. The localisation of GSK-3 within granular structures in pyramidal cells indicates that GSK-3-alpha and GSK-3-beta may have a role in the production of PHF-%%%tau%%% in Alzheimer's disease.

7/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08775326 BIOSIS NO.: 199395064677
Mapping of neurofibrillary degeneration in Alzheimer's disease: Evaluation of heterogeneity using the quantification of abnormal %%%tau%%% proteins.
AUTHOR: Vermersch P; Frigard B; Delacourte A(a)
AUTHOR ADDRESS: (a)Unite INSERM 156, Place de Verdun, F59045 Lille Cedex**
France
JOURNAL: Acta Neuropathologica 85 (1):p48-54 %%%1992%%%
ISSN: 0001-6322
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A biochemical mapping of neurofibrillary degeneration was performed in Brodmann areas of the brains of five patients with senile dementia of the Alzheimer type (AD). To quantify the degenerating process, we used an immunoblot method with antibodies directed against the abnormally %%%phosphorylated%%% %%%tau%%% proteins named %%%Tau%%%
55, 64 and 69, known to be early and reliable markers of the degenerating process in AD. The detection intensities were assessed using a numerical rating scale for each area and scores were grouped by lobe. In all cases, the detection of %%%Tau%%% 55, 64 and 69 was positive in all areas except
in primary visual cortex (area 17) for two patients. The detections were especially strong in temporal neocortical and limbic areas and were higher in associative cortex than in primary sensory cortex. Scores from the occipital and frontal lobes differed strongly between patients as compared to the uniform degree of detection in the limbic, temporal and parietal lobes. Despite a relatively identical duration of the disease and an apparently global involvement of the cerebral cortex, the distribution of neurofibrillary degeneration in AD varies significantly across cortical areas and displays striking heterogeneity patterns along the rostrocaudal axis. The immunodetection of abnormal %%%tau%%% proteins
using the Western blot method may provide complete and rapid quantitative
data of the degenerating process in AD.
? ds

Set Items Description
S1 15749 TAU AND ALZHEIMER?
S2 102 S1 AND PROTEIN(W)SEQUENC?
S3 74 RD S2 (unique items)
S4 19 S3 AND PY<1992
S5 10505 TAU AND PHOSPHORYLAT?
S6 1397 S5 AND PY<1993
S7 602 RD S6 (unique items)
? t s7/7/all

>>>Format 7 is not valid in file 143

Estimated cost of output requested is: $1522.06
Are you ready to receive all output? (Yes/No/Help)
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TYPE Command cancelled.
? s s7 and Alzheimer?

602 S7
247636 ALZHEIMER?
S8 302 S7 AND ALZHEIMER?
? t s8/7/all

>>>Format 7 is not valid in file 143

8/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08787925 BIOSIS NO.: 199395077276
%%%Phosphorylation%%% sites on %%%tau%%% by %%%tau%%% protein kinase I, a
bovine derived kinase generating an epitope of paired helical filaments.
AUTHOR: Ishiguro Koichi(a); Omori Akira; Takamatsu Masako; Sato Kazuki; Arioka Manabu; Uchida Tsuneko; Imahori Kazutomo
AUTHOR ADDRESS: (a)Mitsubishi Kasei Inst. Life Sci., 11 Minamiooya, Machida-shi, Tokyo, 194**Japan
JOURNAL: Neuroscience Letters 148 (1-2):p202-206 %%%1992%%%
ISSN: 0304-3940
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Tau%%% protein kinase I (TPKI) isolated from bovine brain has
been determined to phosphorylte %%%tau%%% at four distinct sites by detecting modified Ser and Thr residues with protein sequencer. Ser199, Thr231, Ser396 and Ser413 were all found to have been %%%phosphorylated%%% by TPKI (numbering of amino acids was done in relation to the longest human %%%tau%%% (Neuron, 3 (1989) 519-526)). These phophorylations generate an epitope of PHF (paired helical filaments) and eliminate the recognition of %%%tau%%% by the monoclonal antibody, %%%tau%%%-1. These results suggested that TPKI might be reponsible for at least some of the %%%phosphorylation%%% of %%%tau%%% to
induce PHF formation

8/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08775405 BIOSIS NO.: 199395064756
Glycogen synthase kinase-3 induces %%%Alzheimer%%%'s disease-like %%%phosphorylation%%% of %%%tau%%%: Generation of paired helical filament
epitopes and neuronal localisation of the kinase.
AUTHOR: Hanger Diane P(a); Hughes Kenneth; Woodgett James R; Brion Jean-Pierre; Anderton Brian H
AUTHOR ADDRESS: (a)Dep. Neurosci., Inst. Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF**UK
JOURNAL: Neuroscience Letters 147 (1):p58-62 %%%1992%%%
ISSN: 0304-3940
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Glycogen synthase kinase-3 (GSK-3) reduced the mobility of human
%%%tau%%% on SDS-PAGE, prevented binding of the monoclonal antibody (mAb), %%%Tau%%%.1, and induced binding of the mAb 8D8. Recombinant %%%tau%%% %%%phosphorylated%%% by GSK-3 aligned on SDS-PAGE with the
abnormally %%%phosphorylated%%% %%%tau%%% (PHF-%%%tau%%%) associated with
the paired helical filaments in %%%Alzheimer%%%'s disease brain.
%%%Phosphorylated%%% serine-396 (numbering of the largest human brain

%%%tau%%% isoform) was identified as a binding site on %%%tau%%% for mAb
8D8. The localisation of GSK-3 within granular structures in pyramidal cells indicates that GSK-3-alpha and GSK-3-beta may have a role in the production of PHF-%%%tau%%% in %%%Alzheimer%%%'s disease.

8/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08775326 BIOSIS NO.: 199395064677
Mapping of neurofibrillary degeneration in %%%Alzheimer%%%'s disease: Evaluation of heterogeneity using the quantification of abnormal %%%tau%%% proteins.
AUTHOR: Vermersch P; Frigard B; Delacourte A(a)
AUTHOR ADDRESS: (a)Unite INSERM 156, Place de Verdun, F59045 Lille Cedex**
France
JOURNAL: Acta Neuropathologica 85 (1):p48-54 %%%1992%%%
ISSN: 0001-6322
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A biochemical mapping of neurofibrillary degeneration was performed in Brodmann areas of the brains of five patients with senile dementia of the %%%Alzheimer%%% type (AD). To quantify the degenerating process, we used an immunoblot method with antibodies directed against the abnormally %%%phosphorylated%%% %%%tau%%% proteins named %%%Tau%%% 55, 64 and 69, known to be early and reliable markers of the degenerating process in AD. The detection intensities were assessed using a numerical rating scale for each area and scores were grouped by lobe. In all cases, the detection of %%%Tau%%% 55, 64 and 69 was positive in all areas except in primary visual cortex (area 17) for two patients. The detections were especially strong in temporal neocortical and limbic areas and were higher in associative cortex than in primary sensory cortex. Scores from the occipital and frontal lobes differed strongly between patients as compared to the uniform degree of detection in the limbic, temporal and parietal lobes. Despite a relatively identical duration of the disease and an apparently global involvement of the cerebral cortex, the distribution of neurofibrillary degeneration in AD varies significantly across cortical areas and displays striking heterogeneity patterns along the rostrocaudal axis. The immunodetection of abnormal %%%tau%%% proteins using the Western blot method may provide complete and rapid quantitative data of the degenerating process in AD.

8/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08775235 BIOSIS NO.: 199395064586
Phosphate analysis and dephosphorylation of modified %%%tau%%% associated with paired helical filaments.
AUTHOR: Ksiezak-Reding Hanna(a); Liu Wan-Kyng; Yen Shu-Hui(a)
AUTHOR ADDRESS: (a)Dep. Pathol., Rm. 538, Albert Einstein Coll. Med., 1300 Morris Park Ave., Bronx, N.Y. 10461**USA
JOURNAL: Brain Research 597 (2):p209-219 %%%1992%%%
ISSN: 0006-8993
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We performed phosphate analysis of %%%tau%%% proteins isolated from normal human brain, %%%tau%%% proteins associated with paired helical filaments (PHF-%%%tau%%%), and %%%Alzheimer%%% %%%tau%%% not associated with PHF. These %%%tau%%% fractions were of high purity. Normal and %%%Alzheimer%%% %%%tau%%% were purified by heat treatment, acid extraction and calmodulin-affinity chromatography with or without HPLC. Fractions containing primarily PHF-%%%tau%%% polypeptides of 60, 64 and 68 kDa and their degraded fragments were purified either on a sucrose density gradient as filaments (PHF) or by heat treatment and acid extraction as amorphous proteins (PHF-%%%tau%%%). PHF and PHF-%%%tau%%% were found to contain 6-8 mol phosphate/mol protein while normal and %%%Alzheimer%%% %%%tau%%% proteins contained 1.9 and 2.6 mol phosphate/mol protein, respectively. Upon 2-h incubation with alkaline phosphatase, PHF lost two of the phosphate groups without apparent changes in the stability and morphology of PHF. The released phosphate originated from the N-terminal half of PHF-%%%tau%%% as determined by immunoblotting with antibodies to epitopes blocked by %%%phosphorylation%%%, %%%Tau%%%-1 and E-2, and by a prominent shift in the electrophoretic mobility of some fragments of PHF-%%%tau%%%. The shift in mobility was not observed with the C-terminal fragments of 25-26 kDa, which retained the epitope to %%%Tau%%% 46. The results suggest that the %%%phosphorylation%%% sites not affected by phosphatase may be located in the 25-26 kDa C-terminal region of PHF-%%%tau%%% and may play a role in structural stability of PHF.

8/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08775192 BIOSIS NO.: 199395064543
Glycogen synthase kinase-3 and the %%%Alzheimer%%%-like state of microtubule-associated protein %%%tau%%%.
AUTHOR: Mandelkow E M(a); Drewes G; Biernat J; Gustke N; Van Lint J; Vandenheede J R; Mandelkow E
AUTHOR ADDRESS: (a)Max-Planck-Unit Structural Molecular Biology, c/o DESY, Nortkestrasse 85, D-2000 Hamburg 52**Germany
JOURNAL: FEBS (Federation of European Biochemical Societies) Letters 314 (3):p315-321 %%%1992%%%
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The %%%Alzheimer%%%-like state of %%%tau%%% protein includes %%%phosphorylation%%% by a proline-directed Ser/Thr kinase present in normal or pathological human brain. Extending earlier results on MAP kinase, we show here that the proline-directed kinase, GSK3, can induce an %%%Alzheimer%%%-like immune response involving several distinct and %%%phosphorylatable%%% epitopes at Ser-Pro motifs, as well as a gel mobility shift, similar to MAP kinase. Both kinases behave like microtubule-associated proteins in that they co-purify through cycles of assembly and disassembly, and both kinases are directly associated with paired helical filaments.

8/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08763834 BIOSIS NO.: 199395053185
Differential %%%phosphorylation%%% of %%%tau%%% by cyclic AMP-dependent protein kinase and calcium/calmodulin-dependent protein kinase II: Metabolic and functional consequences.
AUTHOR: Johnson Gail V W
AUTHOR ADDRESS: Johnson at Sparks Cent., Room 1011, Univ. Alabama at Birmingham, Birmingham, Ala. 35294-0017**
JOURNAL: Journal of Neurochemistry 59 (6):p2056-2062 %%%1992%%%

ISSN: 0022-3042
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The effects of cyclic AMP-dependent protein kinase (cAMP-PK) or
Ca-2+/calmodulin-dependent protein kinase II (CaMKII)
%%%phosphorylation%%% on the binding of bovine %%%tau%%% to tubulin and
calpain-mediated degradation of %%%tau%%% were studied. Both cAMP-PK and
CaMKII readily %%%phosphorylated%%% %%%tau%%% and slowed the migration of
%%%tau%%% on sodium dodecyl sulfate-containing polyacrylamide gels.
However, cAMP-PK %%%phosphorylated%%% %%%tau%%% to a significantly
greater extent than CaMKII (1.5 and 0.9 mol of 32P/mol of %%%tau%%%,
respectively), and %%%phosphorylation%%% of %%%tau%%% by cAMP-PK resulted
in a greater shift to a more acidic, less heterogeneous pattern on
two-dimensional nonequilibrium pH gradient gels compared with CaMKII
%%%phosphorylation%%%. Two-dimensional phosphopeptide maps indicate that
cAMP-PK %%%phosphorylates%%% a site or sites on %%%tau%%% that are
%%%phosphorylated%%% by CaMKII, as well as a unique site or sites that
are not %%%phosphorylated%%% by CaMKII. %%%Phosphorylation%%% of
%%%tau%%% by cAMP-PK significantly decreased tubulin binding and, as
previously reported, also inhibited the calpain-induced degradation of
%%%tau%%%. CaMKII %%%phosphorylation%%% of %%%tau%%% did not alter either
of these parameters. These results suggest that the %%%phosphorylation%%%
of site(s) on the %%%tau%%% molecule uniquely accessible to cAMP-PK
contributed to the decreased %%%tau%%%-tubulin binding and increased
resistance to calpain hydrolysis.

8/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08763629 BIOSIS NO.: 199395052980
Immunocytochemistry of neurofibrillary tangles with antibodies to
subregions of %%%tau%%% protein: Identification of hidden and cleaved
%%%tau%%% epitopes and a new %%%phosphorylation%%% site.
AUTHOR: Dickson D W(a); Ksiezak-Reding H; Liu W-K; Davies P; Crowe A; Yen
S-H C
AUTHOR ADDRESS: (a)Dep. Pathol., Rose F. Kennedy Cent. Res. Mental
Retardation Human Development, Albert Einstein C**USA
JOURNAL: Acta Neuropathologica 84 (6):p596-605 %%%1992%%%
ISSN: 0001-6322
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Antibodies to multiple epitopes spanning the length of the
%%%tau%%% molecule were used to study %%%Alzheimer%%% neurofibrillary
tangles (NFT) using immunocytochemical methods and several different
methods of fixation and tissue processing, including staining of
vibratome sections, hydrated autoclaving of paraffin sections and
immunofluorescence of NFT isolated from fresh brain tissue. Smears and
sections were pretreated with trypsin and/or phosphatase to further
characterize antibody binding. In tissue fixed briefly in
periodate-lysine-paraformaldehyde, %%%tau%%% immunoreactivity was
detected in astrocytes, but only a few %%%tau%%% epitopes were detected
in NFT with this fixation method. In contrast, all %%%tau%%% epitopes
were detected in NFT in tissue fixed in formaldehyde for prolonged
periods of time. In the hippocampus, the number of NFT detected in the
dentate fascia was in proportion to the duration of dementia, as we
previously noted. Dentate fascia NFT were intracellular (i-NFT) and were
reactive with antibodies recognizing epitopes in both the carboxy- and
amino-terminal regions of %%%tau%%%, but not the microtubule-binding
domain of %%%tau%%%, suggesting that microtubule-binding domain epitopes
are hidden in i-NFT. In contrast, NFT in the subiculum and layer II of
the parahippocampal cortex were mostly extracellular (e-NFT), especially
in severe cases of long duration. e-NFT were immunoreactive with
antibodies to the microtubule-binding domain, but only weakly reactive
with antibodies to carboxy- or amino-terminal epitopes, suggesting that
e-NFT may contain fragments of %%%tau%%%. In both isolated NFT and NFT in
sections, amino-terminal epitopes, including the Alz-50 epitope, were
sensitive to trypsin proteolysis, which suggests that te lack of staining
of e-NFT by antibodies to the amino-terminal regions of %%%tau%%% is due
to proteolysis. Antibodies reactive with amino-terminal episopes also
stained fewer NFT following hydrated autoclaving, while those reacting
with the carboxy half of %%%tau%%% stained more NFT after hydrated
autoclaving. Thus, although carboxy-terminal regions are not detected in
e-NFT, they are probably masked, rather than proteolytically cleaved,
since they can be revealed by hydrated autoclaving. Finally, phosphatase
treatment of isolated NFT revealed enhanced immunostaining not only with
%%%Tau%%%-1, as in previous studies demonstrating abnormal
%%%phosphorylation%%% of %%%tau%%% protein in NFT, but also with an
antibody to exon 2, which reveals yet another %%%phosphorylation%%% site
in %%%tau%%% of NFT.

8/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08751988 BIOSIS NO.: 199395041339
%%%Tau%%% pathology in a case of familial %%%Alzheimer%%%'s disease with a
valine to glycine mutation at position 717 in the amyloid precursor
protein.
AUTHOR: Hanger Diane P; Mann David M A; Neary David; Anderton Brian H(a)
AUTHOR ADDRESS: (a)Dep. Neurosci., Inst. Psychiatry, de Crespigny Park,
London SE5 8AF**UK
JOURNAL: Neuroscience Letters 145 (2):p178-180 %%%1992%%%
ISSN: 0304-3940
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The brain tissue from a case of familial %%%Alzheimer%%%'s
disease (FAD) caused by a missense (valine to glycine) mutation at codon
717 of the amyloid precursor protein (APP) gene has been examined for the
presence of abnormality %%%phosphorylated%%% paired helical filament
%%%tau%%% (PHF-%%%tau%%%). There was abundant PHF-%%%tau%%% present,
which on Western blots, was indistinguishable from the PHF-%%%tau%%%
typical of cases of sporadic %%%Alzheimer%%%'s disease and that of
another FAD mutation (valine to isoleucine), previously described
(Neurosci. Lett., 137 (1992) 221-224). This result implies that the
cytoskeletal pathology in %%%Alzheimer%%%'s disease is biochemically
linked to abnormal APP processing and amyloid deposition.

8/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08751985 BIOSIS NO.: 199395041336
P42 map kinase %%%phosphorylation%%% sites in microtubule-associated
protein %%%tau%%% are dephosphorylated by protein phosphatase 2A-1:
Implications for %%%Alzheimer%%%'s disease.
AUTHOR: Goedert Michel(a); Cohen E Suzanne; Jakes Ross; Cohen Philip
AUTHOR ADDRESS: (a)MRC Lab. Molecular Biology, Hills Road, Cambridge CB2
2QH**UK
JOURNAL: FEBS (Federation of European Biochemical Societies) Letters 312 (

1):p95-99 %%%1992%%%
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The paired helical filament (PHF), which comprises the major fibrous element of the neurofibrillary tangle of %%%Alzheimer%%%'s disease, is composed of abnormally %%%phosphorylated%%% microtubule-associated protein %%%tau%%%. Here we show that p42 MAP kinase %%%phosphorylates%%% recombinant %%%tau%%% and converts it to a form which is similar to PHF %%%tau%%%. Of the major serine/threonine protein phosphatases found in mammalian tissues only protein phosphatase 2A (PP2A) could dephosphorylate %%%tau%%% %%%phosphorylated%%% in this manner, with PP2A-1 being the most effective form of the enzyme.

8/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08740909 BIOSIS NO.: 199395030260
Proline-directed %%%phosphorylation%%% of human %%%tau%%% protein.
AUTHOR: Vulliet Richard(a); Halloran S Mitchell; Braun Ruedi K; Smith Alan J; Lee Gloria
AUTHOR ADDRESS: (a)Dep. Vet. Pharmacol. Toxicol., Univ. Calif., Davis, Calif. 95616**ussia
JOURNAL: Journal of Biological Chemistry 267 (31):p22570-22574 %%%1992%%%
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The primary sequence of the microtubule-associated proetin %%%tau%%% contains multiple repeats of the sequence -X-Ser-/Thr-Pro-X-, the consensus sequence for the proline-directed protein kinase (p34-cdc2/p58-cyclin A). When %%%phosphorylated%%% by proline-directed protein kinase in vitro, %%%tau%%% was found to incorporate up to 4.4 mol of phosphate/mol of protein. Isoelectric focusing of the tryptic phosphopeptides demonstrated the presence of five distinct peptides with pI values of approximately 6.9, 6.5, 5.6-5.9, 4.7, and 3.6. Mapping of the tryptic phosphopeptides by high performance liquid chromatography techniques demonstrated three distinct peaks. Data from gas phase sequencing, amino acid analysis, and phosphoamino acid analysis suggest that proline-directed protein kinase %%%phosphorylates%%% %%%tau%%% at four sites. Each site demonstrates the presence of a proline residue on the carboxyl-terminal side of the %%%phosphorylated%%% residue. Two %%%phosphorylation%%% sites are located adjacent to the three-repeat microtubule-binding domain that has been found to be required for the in vivo co-localization of %%%tau%%% protein to microtubules. Two other putative %%%phosphorylation%%% sites are located within the identified epitope of the monoclonal antibody %%%Tau%%%-1. %%%Phosphorylation%%% of these sites altered the immunoreactivity of %%%tau%%% to %%%Tau%%%-1 antibody. Since the neuronal microtubule-associated protein %%%tau%%% is multiply %%%phosphorylated%%% in %%%Alzheimer%%%'s disease, and %%%Tau%%% -1 immunoreactivity is similarly reduced in neurofibrillary tangles and enhanced after dephosphorylation, phosphophorylation at one or more of three sites may correlate with abnormally %%%phosphorylated%%% sites in %%%tau%%% protein in %%%Alzheimer%%%'s disease.

8/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08729888 BIOSIS NO.: 199395019239
A serine fwdarw proline change in the %%%Alzheimer%%%'s disease-associated epitope %%%Tau%%%-2 results in altered secondary structure, but %%%phosphorylation%%% overcomes the conformational gap.
AUTHOR: Lang Emma; Otvos Laszlo Jr(a)
AUTHOR ADDRESS: (a)Wistar Institute Anatomy Biology, 3601 Spruce Street, Philadelphia, Pa. 19104
JOURNAL: Biochemical and Biophysical Research Communications 188 (1):p162-169 %%%1992%%%
ISSN: 0006-291X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Monoclonal antiboddy %%%Tau%%% 2 was raised against bovine %%%tau%%% protein, was reported to recognize a conformational epitope, and stained %%%tau%%% was found in neurofibrillary tangles of %%%Alzheimer%%%'s disease, but not normal human %%%tau%%%. We synthesized tetradeka peptides corresponding to the original bovine sequence, its serine fwdarw proline substitued analog, the genuine human sequence of this region, and the bovine epitope %%%phosphorylated%%% on the crucial serine. The secondary structure of the peptides was determined by circular dichroism. It was found that only the original bovine epitope showed a tendency to form the beta-pleated sheets characteristic of the neurofibrillary tangles. The spectra of the human peptide, it analog, and the %%%phosphorylated%%% bovine sequence were very similar, featuring a weak, helical beta-turn character. Eventual %%%phosphorylation%%% of epitopes of this otherwise heavily %%%phosphorylated%%% protein may overcome inter-species conformational gaps.

8/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08717933 BIOSIS NO.: 199395007284
Presence of abnormally %%%phosphorylated%%% %%%Tau%%% proteins in the entorhinal cortex of aged non-demented subjects.
AUTHOR: Vermersch Patrick; Frigard Bernard; David Jean-Philippe; Fallet-Bianco Catherine; Delacourte Andre(a)
AUTHOR ADDRESS: (a)INSERM U156, Place de Verdun, 59045 Lille cedex**France
JOURNAL: Neuroscience Letters 144 (1-2):p143-146 %%%1992%%%
ISSN: 0304-3940
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An inmmunoblot study was performed in several cortical samples from non-demented aged controls and compared with those from %%%Alzheimer%%% patients, using antibodies against %%%Tau%%% 55, 64 and 69, which are specific and reliable markers of the neurofibrillary degeneration of the %%%Alzheimer%%% type. The immunodetection of %%%Tau%%% 55, 64 and 69 was positive in all cortical areas from %%%Alzheimer%%% patients, in the entorhinal cortex from each control aged more than 65 but not in cortical samples from younger controls. We demonstrate that the entorhinal cortex is the most vulnerable neuronal population in aging and that the biochemical dysfunctions observed in this area are typically of the '%%%Alzheimer%%%-type'.

8/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08717649 BIOSIS NO.: 199395007000
Immunological and conformational characterization of a %%%phosphorylated%%%

immunodominant epitope on the paired helical filaments found in %%%Alzheimer%%%'s disease.
AUTHOR: Lang Emma; Szendrei Gyorgyi I; Lee Virginia M-Y; Otvos Laszlo Jr(a)
AUTHOR ADDRESS: (a)Wistar Institute Anatomy Biology, 3601 Spruce Street,
Philadelphia, Pa. 19104
JOURNAL: Biochemical and Biophysical Research Communications 187 (2):p783-790 %%%1992%%%
ISSN: 0006-291X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The immunological recognition pattern of one of the most commonly
used monoclonal antibodies, PHF-1, which detects the paired helical filaments of %%%Alzheimer%%%'s disease, exhibits a high degree of similarity with the recognition of a polyclonal antibody, anti-T3P, raised against a synthetic phosphopeptide, GAEIVYKS(Phospho)PVVSGD, corresponding to amino acids 389-402 of the microtubule-associated protein %%%tau%%%. A panel of 16 synthetic non-%%%phosphorylated%%% and
%%%phosphorylated%%% peptides, excised from different regions of %%%tau%%% and peptide analogs thereof, were used to show that PHF-1 is
indeed directed against the T3 fragment. Circular dichroism spectroscopy shows that the %%%phosphorylated%%% peptide exhibits a limited propensity
to form intramolecular beta-pleated sheets, and alteration is found in the reverse-turn structure that dominates the middle section of the molecule. The shift in the turn-forming amino acids may also allow a stacking procedure, may interfere with microtubule assembly, and, consequently, may be accountable for deposit formation.

8/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08500932 BIOSIS NO.: 199344050932
The %%%Alzheimer%%%-like state of %%%tau%%% protein: Kinases and %%%phosphorylation%%% sites.
AUTHOR: Mandelkow E-M(a); Biernat J; Lichtenberg-Kraag B; Steiner B; Wille
H; Drewes G; Gustke N; Meyer H; Goedert M; Mandelkow E
AUTHOR ADDRESS: (a)Max-Planck-Unit Struct. Mol. Biol., D-2000 Hamburg 52**
Germany
JOURNAL: Society for Neuroscience Abstracts 18 (1-2):p563 %%%1992%%%
CONFERENCE/MEETING: 22nd Annual Meeting of the Society for Neuroscience
Anaheim, California, USA October 25-30, 1992
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English

8/7/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08500930 BIOSIS NO.: 199344050930
%%%Phosphorylation%%% states of bovine %%%tau%%%, porcine %%%tau%%%, and a
%%%tau%%% fragment bound to %%%Alzheimer%%% PHFs.
AUTHOR: Scott C W(a); Poulter L; Barratt D; Wischik C; Caputo C B
AUTHOR ADDRESS: (a)ICI Americas Inc., Wilmington, Del. 19897
JOURNAL: Society for Neuroscience Abstracts 18 (1-2):p563 %%%1992%%%
CONFERENCE/MEETING: 22nd Annual Meeting of the Society for Neuroscience
Anaheim, California, USA October 25-30, 1992
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English

8/7/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08500929 BIOSIS NO.: 199344050929
%%%Phosphorylation%%%, calpain hydrolysis and tubulin binding of the recombinant human %%%tau%%% isoform, T3.
AUTHOR: Litersky J M(a); Greenwood J A; Scott C W; Johnson G V W
AUTHOR ADDRESS: (a)Dep. Psychiatry, Univ. Ala., Birmingham, Ala. 35294-0017
JOURNAL: Society for Neuroscience Abstracts 18 (1-2):p562 %%%1992%%%
CONFERENCE/MEETING: 22nd Annual Meeting of the Society for Neuroscience
Anaheim, California, USA October 25-30, 1992
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English

8/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08500928 BIOSIS NO.: 199344050928
Casein kinase II %%%phosphorylation%%% of %%%tau%%% and MAP-2.
AUTHOR: Greenwood J A; Johnson G V W
AUTHOR ADDRESS: Dep. Psychiatry, Univ. Ala., Brimingham, Ala. 35294-0017**
JOURNAL: Society for Neuroscience Abstracts 18 (1-2):p562 %%%1992%%%
CONFERENCE/MEETING: 22nd Annual Meeting of the Society for Neuroscience
Anaheim, California, USA October 25-30, 1992
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English

8/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

08500927 BIOSIS NO.: 199344050927
The abnormal %%%phosphorylation%%% of %%%tau%%% at SER396 in %%%Alzheimer%%%'s disease recapitulates %%%phosphorylation%%% during
development and contributes to reduced microtubule binding.
AUTHOR: Merrick S E(a); Bramblett G T; Goedert M; Jakes R; Trojanowski J Q;
Lee V M-Y
AUTHOR ADDRESS: (a)Dep. Pathol., Inst. Neurosci., Univ. Pa., Philadelphia, Pa. 19104
JOURNAL: Society for Neuroscience Abstracts 18 (1-2):p562 %%%1992%%%
CONFERENCE/MEETING: 22nd Annual Meeting of the Society for Neuroscience
Anaheim, California, USA October 25-30, 1992
ISSN: 0190-5295
RECORD TYPE: Citation
LANGUAGE: English

8/7/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08485479 BIOSIS NO.: 199344035479
The pathology of the neuronal cytoskeleton in %%%Alzheimer%%%'s disease.
AUTHOR: Brion Jean-Pierre
AUTHOR ADDRESS: Lab. Pathol. Electron Microscopy, Universite Libre de Bruxelles 808, Route de Lennik, Building C-10,**Belgium

JOURNAL: Biochimica et Biophysica Acta 1160 (1):p134-142 %%%1992%%%
CONFERENCE/MEETING: Second European Symposium on Calcium-Binding Proteins
in Normal and Transformed Cells Marseilles, France March 1-6, 1992
ISSN: 0006-3002
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English

8/7/20 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08482027 BIOSIS NO.: 199344032027
Molecular pathology of %%%Alzheimer%%% neurofibrillary degeneration.
AUTHOR: Lqbal Khalid; Grundke-Iqbal Inge
AUTHOR ADDRESS: New York State Inst., Basic Res. Dev. Disabilites, Staten
Island, N.Y. 10314**USA
JOURNAL: Acta Neurobiologiae Experimentalis (Warsaw) 52 (3):p124 %%%1992%%%
CONFERENCE/MEETING: First International Congress of the Polish Neuroscience
Society, Part I Warsaw, Poland September 21-23, 1992
ISSN: 0065-1400
RECORD TYPE: Citation
LANGUAGE: English

8/7/21 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08471384 BIOSIS NO.: 199344021384
Interaction of neurofilament antibodies with %%%tau%%% protein and relationship with %%%Alzheimer%%% %%%tau%%%.
AUTHOR: Lichtenberg-Kraag B(a); Mandelkow E-M(a); Biernat J(a); Steiner B
(a); Schroeter C(a); Gustke N(a); Meyer H E; Lkow Mande(a)
AUTHOR ADDRESS: (a)Max-Planck-Unit Structural Molecular Biol., c/o DESY,
Notkestrasse 85, D-2000 Hamburg 52**Germany
JOURNAL: Biological Chemistry Hoppe-Seyler 373 (9):p794-795 %%%1992%%%
CONFERENCE/MEETING: Autumn Meeting of the Gesellschaft fuer Biologische
Chemie (German Society for Biological Chemistry), Rostock, Germany, September 24-26, 1992. BIOL CHEM HOPPE-SEYLER
ISSN: 0177-3593
RECORD TYPE: Citation
LANGUAGE: English

8/7/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08471319 BIOSIS NO.: 199344021319
%%%Phosphorylation%%% of the serine-proline motifs transforms normal %%%tau%%% protein into an %%%Alzheimer%%%-like state and reduces its
microtubule binding.
AUTHOR: Gustke N(a); Steiner B(a); Mandelkow E-M(a); Biernat J(a); Meyer H
E; Goedert H; Mandelkow E(a)
AUTHOR ADDRESS: (a)Max-Planck-Unit Struct., Mol. Biol., c/o DESY, Notkestr.
85, D-2000 Hamburg 52**Germany
JOURNAL: Biological Chemistry Hoppe-Seyler 373 (9):p772 %%%1992%%%
CONFERENCE/MEETING: Autumn Meeting of the Gesellschaft fuer Biologische
Chemie (German Society for Biological Chemistry), Rostock, Germany, September 24-26, 1992. BIOL CHEM HOPPE-SEYLER
ISSN: 0177-3593
RECORD TYPE: Citation
LANGUAGE: English

8/7/23 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08471263 BIOSIS NO.: 199344021263
The switch of %%%tau%%% protein to an %%%Alzheimer%%%-like state includes
the %%%phosphorylation%%% of two serine-proline motifs upstream of the
microtubule binding region.
AUTHOR: Biernat J(a); Mandelkow E-M(a); Schroeter C(a); Lichtenberg-Kraag B
(a); Steiner B(a); Berling B(a); Meyer H E; Mercken M; Vandermeeren A; et al
AUTHOR ADDRESS: (a)Max-Planck-Unit Struct. Mol. Biol., c/o DESY,
Notkestrasse 85, D-2000 Hamburg 52**Germany
JOURNAL: Biological Chemistry Hoppe-Seyler 373 (9):p753 %%%1992%%%
CONFERENCE/MEETING: Autumn Meeting of the Gesellschaft fuer Biologische
Chemie (German Society for Biological Chemistry), Rostock, Germany, September 24-26, 1992. BIOL CHEM HOPPE-SEYLER
ISSN: 0177-3593
RECORD TYPE: Citation
LANGUAGE: English

8/7/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08456648 BIOSIS NO.: 199344006648
In vivo analysis of PDPK %%%phosphorylation%%% sites on %%%tau%%% protein.
AUTHOR: Leger J G; Lee G
AUTHOR ADDRESS: Center Neurol. Diseases, Brigham and Women's Hospital,
Harvard Med. Sch., Boston, Mass. 02115**Germany
JOURNAL: Molecular Biology of the Cell 3 (SUPPL.):p164A %%%1992%%%
CONFERENCE/MEETING: Thirty-second Annual Meeting of the American Society
for Cell Biology, Denver, Colorado, USA, November 15-19, 1992. MOL BIOL CELL
ISSN: 1059-1524
RECORD TYPE: Citation
LANGUAGE: English

8/7/25 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08456646 BIOSIS NO.: 199344006646
Recombinant MAP kinase from brain %%%phosphorylates%%% %%%tau%%% protein
similar to %%%tau%%% from %%%Alzheimer%%% paired helical filaments.
AUTHOR: Berling B; Doering F; Drewes G; Mandelkow E M
AUTHOR ADDRESS: Maxk-Planck Unit Struct. Mol. Biol., D-2000 Hamburg 52**
Germany
JOURNAL: Molecular Biology of the Cell 3 (SUPPL.):p164A %%%1992%%%
CONFERENCE/MEETING: Thirty-second Annual Meeting of the American Society
for Cell Biology, Denver, Colorado, USA, November 15-19, 1992. MOL BIOL CELL
ISSN: 1059-1524
RECORD TYPE: Citation
LANGUAGE: English

8/7/26 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08456644 BIOSIS NO.: 199344006644
%%%Phosphorylation%%% dependent antibody epitopes on %%%tau%%% protein and
relationship with the %%%Alzheimer%%%-like state of %%%tau%%%.
AUTHOR: Biernat J; Mandelkow E-M; Lichtenberg-Kraag B; Steiner B; Schroeter
C; Gustke N; Meyer H E; Mercken M; Vandermeeren A; et al
AUTHOR ADDRESS: Max-Planck Unit Struct. Mol. Biol., D-2000 Hamburg 52**
Germany
JOURNAL: Molecular Biology of the Cell 3 (SUPPL.):p164A %%%1992%%%
CONFERENCE/MEETING: Thirty-second Annual Meeting of the American Society
for Cell Biology, Denver, Colorado, USA, November 15-19, 1992. MOL BIOL CELL
ISSN: 1059-1524
RECORD TYPE: Citation
LANGUAGE: English

8/7/27 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08428949 BIOSIS NO.: 000094136153
TREATMENT OF %%%ALZHEIMER%%%'S DISEASE BY ZINC COMPOUNDS
AUTHOR: CONSTANTINIDIS J
AUTHOR ADDRESS: UNIV. PSYCHIATRIC INST., BEL-AIR, CH-1225 GENEVA, SWITZ.
JOURNAL: DRUG DEV RES 27 (1). 1992. 1-14. %%%1992%%%
FULL JOURNAL NAME: Drug Development Research
CODEN: DDRED
DOCUMENT TYPE: Review
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: At the onset of %%%Alzheimer%%%'s disease (AD), specific lesions
occur in the hippocampus, i.e., neuropile-capillary amyloid (AM) plaques and neuronal paired-helical filaments (PHF)-neurofibrillary tangles (NFT). The hippocampus is the area of brain with the highest zinc content. Chemical investigations demonstrated that in AD, the cerebral zinc decreases, especially in the hippocampus. The mechanism may be the following: The primary, genetically determined, microvascular AM (asymptomatic) disturbs the blood-brain barrier, and metals (calcium, iron, aluminium, silicon, mercury, etc.) reach the cerebral cortex, where their levels increase and displace the zinc (whose level decreases) in some enzymes which become nonfunctional. The secondary production of PHF-NFT and the neuronal dysfunction responsible of the clinical symptoms of dementia may be related to the functional deficiency of the following zinc-enzymes: 1) those of DNA metabolism giving rise to abnormal DNA and therefore synthesis of abnormal proteins, constituting the NFT; 2) those involved in %%%phosphorylating%%% mechanisms at a post-transcriptional (ribosomal-mitochondrial) level, producing the abnormally %%%phosphorylated%%% %%%tau%%% protein, constituting the PHF; 3) that of
glutamate (GLU) catabolism, resulting in a neurotoxic increase of GLU, producing PHF by abnormal %%%phosphorylation%%% of the neurofilaments; 4)
those of neuronal detoxification contributing to the neuronal dysfunction. In regard to potential for therapeutic intervention, the timing needed for the AM-induced production of NFT, in the various areas of the brain, has been estimated to be about 14-67 months. During this time it may be possible to influence the AM-induced production of NFT: The chronic administration of neuroleptics enhances it, and the chronic administration of other drugs may reduce it. Such drugs may be zinc compounds, which will give an excess of zinc in the brain, will inhibit the above-mentioned AM induced by zinc deficiency, mechanisms producing the NFT related to the clinical symptoms of dementia, and therefore, may prevent, stop, delay, and even improve them. Preliminary trials with zinc-aspartate give promising results. Research is in progress to consolidate this zinc theory and to find more appropriate zinc compounds for this treatment.

8/7/28 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08427335 BIOSIS NO.: 000094134539
%%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEIN BY PURIFIED P34C-D-C-28 AND A
RELATED PROTEIN KINASE FROM NEUROFILAMENTS
AUTHOR: MAWAL-DEWAN M; SEN P C; ABDEL-GHANY M; SHALLOWAY D; RACKER E
AUTHOR ADDRESS: SECTION BIOCHEMISTRY MOLECULAR CELL BIOLOGY, CORNELL UNIV.,
ITHACA, NEW YORK 14853.
JOURNAL: J BIOL CHEM 267 (27). 1992. 19705-19709. %%%1992%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: It has been suggested that hyperphosphorylation of the %%%tau%%%
protein in neurofibrillary tangles may be relevant to the etiology of %%%Alzheimer%%%'s disease and that at least one of the hyperphosphorylated sites lies within a consensus sequence from the p34cdc2/cdc28 family of kinases. We describe a new method for large-scale
purification of p34cdc28 kinase from Saccharomyces cerevisiae and show that the purified enzyme can %%%phosphorylate%%% bovine and human %%%tau%%%. %%%Phosphorylation%%% was greatly enhanced by the addition of
basic and acidic substrate modulators. The effect of the substrate modulators differed both with the structures of the substrates and the modulators. Similar results were obtained with a kinase that could be purified from neurofilaments by p13suc1 affinity chromatography, a hallmark of p34cdc2/cdc28-type kinases. These results are consistent with the hypothesis that a kinase of this type is involved in %%%tau%%% %%%phosphorylation%%% in vivo and open the possibility that hyperphosphorylation in %%%Alzheimer%%%'s disease may be controlled by
substrate modulators.

8/7/29 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08427296 BIOSIS NO.: 000094134500
MONOCLONAL ANTIBODIES WITH SELECTIVE SPECIFICITY FOR %%%ALZHEIMER%%%
%%%TAU%%% ARE DIRECTED AGAINST PHOSPHATASE-SENSITIVE EPITOPES
AUTHOR: MERCKEN M; VANDERMEEREN M; LUEBKE U; SIX J; BOONS J; VAN DE VOORDE
A; MARTIN J-J; GHEUENS J
AUTHOR ADDRESS: LABORATORY MOLECULAR NEUROSCIENCE AGING RESEARCH, MAILMAN
RESEARCH CENTER, MCLEAN HOSPITAL, BELMONT, MASS. 02178, USA.
JOURNAL: ACTA NEUROPATHOL 84 (3). 1992. 265-272. %%%1992%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A modified form of the microtubule-associated protein %%%Tau%%%
is the major component of the paired helical filaments (PHF) found in %%%Alzheimer%%%'s disease. The characterization of these posttranslational %%%Tau%%% modifications is hindered by the lack of sufficient PHF-%%%Tau%%%-specific markers. Here we describe several monoclonal antibodies, prepared by immunization with PHF, two of which showed a selective specificity for PHF-%%%Tau%%% without cross-reactivity
with normal %%%Tau%%%. Epitope recognition by these two monoclonals was
sensitive to alkaline phosphatase treatment. In Western blotting these

monoclonal antibodies reacted specifically with the abnormally %%%phosphorylated%%% epitopes on %%%Alzheimer%%%'s disease-associated PHF-%%%Tau%%%. One of the new antibodies can be used for the construction of a sandwich enzyme-linked immunosorbent assay for the specific detection of PHF-%%%Tau%%% without cross-reactivity to normal %%%Tau%%% proteins.

8/7/30 (Item 30 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08405595 BIOSIS NO.: 000094123249
%%%TAU%%% AND UBIQUITIN IN THE HUMAN HYPOTHALAMUS IN AGING AND %%%ALZHEIMER%%%'S DISEASE
AUTHOR: SWAAB D F; GRUNDKE-IQBAL I; IQBAL K; KREMER H P H; RAVID R; VAN DE NES J A P
AUTHOR ADDRESS: NETHERLANDS INST. BRAIN RESEARCH, MEIBERGDREEF 33, 1105 AZ AMSTERDAM-ZUIDOOST, NETHERLANDS.
JOURNAL: BRAIN RES 590 (1-2). 1992. 239-249. %%%1992%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Immunocytochemical staining of hypothalamic cell groups with four antibodies to %%%Alzheimer%%% paired helical filaments (PHF) (i.e., anti-PHF serum 60e and monoclonal antibody (mAb) Alz-50, both directed against normal and abnormally %%%phosphorylated%%% .%%%tau%%%.: mAb . %%%tau%%%.-1, which recognizes .%%%tau%%%.; and mAb 3-39 to PHF, which recognizes the carboxy terminal domain of ubiquitin) revealed a clear distinction between 12 %%%Alzheimer%%%'s disease (AD) patients and seven controls in the hypothalamus. Dystrophic neurites, which appeared to be the most specific components in AD, were most conspicuous after Alz-50 staining. Alz-50 also stained neuronal cytoplasm and normal, thin, beaded neurites in the paraventricular nucleus (PVN) of controls, even of young cases. This staining was clearly distinct from the staining of cytoplasm and dystrophic neurites in the PVN of %%%Alzheimer%%% patients. The abundant staining of dystrophic neurites and cell bodies in the nucleus tuberalis lateralis (NTL) in AD, in which no neuronal loss is observed, suggests that alterations in cytoskeletal markers do not necessarily indicate impending cell death. Moreover, the cytoskeletal changes in the NTL, sexually dimorphic and suprachiasmatic nuclei in AD indicate that this condition is not restricted to cortical areas of nuclei projecting to the cortex. Consequently, the pathophysiological implications of cytoskeletal staining in AD are at present far from clear. The human hypothalamus may not only provide a better insight into the pathogenesis of %%%Alzheimer%%%'s disease, but could also be of help in the neuropathological diagnosis of this condition.

8/7/31 (Item 31 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08405551 BIOSIS NO.: 000094123205
THE MICROTUBULE BINDING REPEATS OF %%%TAU%%% PROTEIN ASSEMBLE INTO FILAMENTS LIKE THOSE FOUND IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: CROWTHER R A; OLESEN O F; JAKES R; GOEDERT M
AUTHOR ADDRESS: MED. RESEARCH COUNCIL, LAB. MOLECULAR BIOL., HILLS RD., CAMBRIDGE CB2 2QH, UK.
JOURNAL: FEBS (FED EUR BIOCHEM SOC) LETT 309 (2). 1992. 199-202. %%%1992%%%
FULL JOURNAL NAME: FEBS (Federation of European Biochemical Societies) Letters
CODEN: FEBLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The paired helical filament, which comprises the major fibrous element of the neurofibrillary tangle in %%%Alzheimer%%%'s disease, contains abnormally %%%phosphorylated%%% microtubule-associated protein %%%tau%%% as its principal constituent. The repeat region of %%%tau%%% protein, which represents the microtubule binding domain, forms the core of the filament. Here we show that an expressed fragment of %%%tau%%% protein spanning the repeat region can assemble in vitro into filaments like those found in %%%Alzheimer%%%'s disease.

8/7/32 (Item 32 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08392280 BIOSIS NO.: 000043100609
A DISCUSSION OF THE SIGNIFICANCE OF MUTATIONS IN THE BETA AMYLOID PRECURSOR PROTEIN GENE AS ONE CAUSE OF %%%ALZHEIMER%%%'S DISEASE
AUTHOR: HARDY J
AUTHOR ADDRESS: ALZHEIMER'S DIS. RES. GROUP, ST. MARY'S HOSP. MED. SCH., LONDON, W2 1PG, UK.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL. 1). 1992. S64-S65. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/33 (Item 33 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08392252 BIOSIS NO.: 000043100581
THE EFFECT OF PROTEIN KINASE MODULATORS ON THE LEVEL OF %%%TAU%%% EXPRESSED IN TRANSFECTED CHINESE HAMSTER OVARY CELLS
AUTHOR: TWIST E C; LATIMER D A; ANDERTON B H; GALLO J-M
AUTHOR ADDRESS: DEP. NEUROL., INST. PSYCHIATRY, LONDON, ENGL.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL. 1). 1992. S57. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/34 (Item 34 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08392250 BIOSIS NO.: 000043100579
A-68 ADAP %%%TAU%%% PHF-%%%TAU%%%-P-H-F PATHOLOGICAL %%%TAU%%% %%%PHOSPHORYLATED%%% %%%TAU%%% ROSE BY ANY OTHER NAME?
AUTHOR: GHANBARI H; MILLER B; CHONG J; DAVIES P
AUTHOR ADDRESS: ABBOTT LAB., ABBOTT PARK, ILL.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S

DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S57. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/35 (Item 35 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08392247 BIOSIS NO.: 000043100576
ABNORMALLY %%%PHOSPHORYLATED%%% %%%TAU%%% IS ASSOCIATED WITH DEFECTIVE GTP
BINDING TO THE BETA-SUBUNIT OF TUBULIN IN %%%ALZHEIMER%%% DISEASE BRAIN
AUTHOR: KHATOON S; GRUNDKE-IQBAL I; IQBAL K
AUTHOR ADDRESS: NEW YORK STATE UNIV. INST. BASIC RES. DEV. DISABILITIES,
STATEN ISLAND, N.Y. 10314.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S56. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/36 (Item 36 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08392245 BIOSIS NO.: 000043100574
ABNORMALLY %%%PHOSPHORYLATED%%% %%%TAU%%% IS PRESENT BOTH IN PHF AND
NON-PHF FORMS IN %%%ALZHEIMER%%% DISEASE BRAIN
AUTHOR: KOPKE E; IQBAL K; GRUNDKE-IQBAL I
AUTHOR ADDRESS: INST. BASIC RES. DEV. DISABILITIES, 1050 FOREST HILL RD.,
STATEN ISLAND, N.Y. 10314.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S55-S56. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/37 (Item 37 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08392239 BIOSIS NO.: 000043100568
%%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEIN BY CAMP-DEPENDENT PROTEIN KINASE
IDENTIFICATION OF %%%PHOSPHORYLATION%%% SITES AND EFFECT ON %%%TAU%%%
FUNCTION
AUTHOR: SCOTT C W; SPREEN R C; HERMAN J L; CHOW F H; CAPUTO C B
AUTHOR ADDRESS: ICI PHARM. GROUP, ICI AMERICAS, WILMINGTON, DEL. 19897.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S54. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/38 (Item 38 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08392235 BIOSIS NO.: 000043100564
THE %%%ALZHEIMER%%%-LIKE STATE OF %%%TAU%%% PROTEIN A STUDY OF ISOFORMS
%%%PHOSPHORYLATION%%% SITES ANTIBODY EPITOPES AND PROTEIN KINASES
AUTHOR: MANDELKOW E-M; LICHTENBERG-KRAAG B; STEINER B; BIERNAT J; GUSTKE N;
WILLE H; DREWES G; MEYER H; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANCK-UNIT STRUCT. MOL. BIOL., C/O DESY, NOTKESTR. 85,
D-2000 HAMBURG 52, GER.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S53. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/39 (Item 39 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08392234 BIOSIS NO.: 000043100563
%%%PHOSPHORYLATION%%% OF BOVINE %%%TAU%%% BY MULTIPLE PROTEIN KINASES
AUTHOR: SINGH T J; GRUNDKE-IQBAL I; IQBAL K
AUTHOR ADDRESS: NEW YORK STATE INST. BASIC RES. DEV. DISABILITIES, STATEN
ISLAND, N.Y. 10314.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S53. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/40 (Item 40 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08392230 BIOSIS NO.: 000043100559
ROLE OF ABNORMAL %%%PHOSPHORYLATION%%% OF %%%TAU%%% IN NEURONAL
DEGENERATION
AUTHOR: IQBAL K; GRUNDKE-IQBAL I
AUTHOR ADDRESS: INST. BASIC RES. DEV. DISABILITIES, STATEN ISLAND, N.Y.
10314.
JOURNAL: THIRD INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, ABANO TERME, ITALY, JULY 12-17, 1992. NEUROBIOL AGING 13 (SUPPL.
1). 1992. S52. %%%1992%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/41 (Item 41 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08380549 BIOSIS NO.: 000094111053
PROTEIN SEQUENCE AND MASS SPECTROMETRIC ANALYSES OF %%%TAU%%% IN THE
%%%ALZHEIMER%%%'S DISEASE BRAIN
AUTHOR: HASEGAWA M; MORISHIMA-KAWASHIMA M; TAKIO K; SUZUKI M; TITANI K;
IHARA Y
AUTHOR ADDRESS: DEP. NEUROPATHOLOGY, INSTITUTE BRAIN RESEARCH, FACULTY
MEDICINE, UNIVERSITY TOKYO, 7-3-1 HONGO, BUNKYO, TOKYO 113, JPN.
JOURNAL: J BIOL CHEM 267 (24). 1992. 17047-17054. %%%1992%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% with unusually slow mobilities in sodium dodecyl sulfate-polyacrylamide gel electrophoresis was purified from the Sarkosyl-insoluble pellet of %%%Alzheimer%%%'s disease brain homogenates.
Such species of %%%tau%%% (PHF-%%%tau%%%) are considered to construct the framework of the sodium dodecyl sulfate-soluble form of paired helical filaments (PHF). Detailed comparison of peptide maps of PHF-%%%tau%%% and normal %%%tau%%% before and after dephosphorylation pointed to three anomalously eluted peaks which contained abnormally %%%phosphorylated%%% peptides, residues 191-225, 226-240, 260-267, and 386-438, according to the numbering of the longest %%%tau%%% isoform (Goedert, M., Spillantini, M. G., Jakes, R., Rutherford, D., and Crowther, R. A. (1989) Neuron 3, 519-526). Protein sequence and mass spectrometric analyses localized Thr-231 and Ser-235 as the abnormal %%%phosphorylation%%% sites and further indicated that each %%%tau%%% 1 site (residues 191-225) and the most carboxyl-terminal portion of the protein (residues 386-438) carries more than two abnormal phosphates. Ser-262 was also %%%phosphorylated%%% in a fraction of PHF-%%%tau%%%. Modifications other than %%%phosphorylation%%%, removal of the initiator methionine, and N.alpha.-acetylation at the amino terminus and deamidation at 2 asparaginyl residues were found in PHF-%%%tau%%%, but these modifications were also present in normal %%%tau%%%.

8/7/42 (Item 42 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08380441 BIOSIS NO.: 000094110945
IMPLICATION OF BRAIN CDC2 AND MAP2 KINASES IN THE %%%PHOSPHORYLATION%%% OF
%%%TAU%%% PROTEIN IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: LEDESMA M D; CORREAS I; AVILA J; DIAZ-NIDO J
AUTHOR ADDRESS: CENT. BIOL. MOL., UNIV. AUTONOMA, 28049 MADRID, SPAIN.
JOURNAL: FEBS (FED EUR BIOCHEM SOC) LETT 308 (2). 1992. 218-224. %%%1992%%%
FULL JOURNAL NAME: FEBS (Federation of European Biochemical Societies) Letters
CODEN: FEBLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Brain %%%tau%%% protein is %%%phosphorylated%%% in vitro by cdc2 and MAP2 kinases, obtained through immunoaffinity purification from rat brain extracts. The %%%phosphorylation%%% sites are located on the %%%tau%%% molecule both upstream and downstream of the tubulin-binding motifs. A synthetic peptide comprising residues 194-213 of the %%%tau%%% sequence, which contains the epitope recognized by the monoclonal antibody %%%tau%%%-1, is also efficiently %%%phosphorylated%%% in vitro by cdc2 and MAP2 kinases. %%%Phosphorylation%%% of this peptide markedly reduces its interaction with the antibody %%%tau%%%-1, as it has been described for %%%tau%%% protein in %%%Alzheimer%%%'s disease. Both cdc2 and MAP2 kinases are present in brain extracts obtained from %%%Alzheimer%%%'s disease patients. Interestingly, the level of cdc2 kinase may be increased in patient brains as compared with non-demented controls. These results suggest a role for cdc2 and MAP2 kinases in %%%phosphorylating%%% %%%tau%%% protein at the %%%tau%%%-1 epitope in %%%Alzheimer%%%'s disease.

8/7/43 (Item 43 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08374947 BIOSIS NO.: 000094105451
%%%ALZHEIMER%%%-LIKE PAIRED HELICAL FILAMENTS AND ANTIPARALLEL DIMERS
FORMED FROM MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% IN-VITRO
AUTHOR: WILLE H; DREWES G; BIERNAT J; MANDELKOW E-M; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANCK-UNIT STRUCTURAL MOLECULAR BIOLOGY, C/O DESY,
D-2000 HAMBURG 52, GER.
JOURNAL: J CELL BIOL 118 (3). 1992. 573-584. %%%1992%%%
FULL JOURNAL NAME: Journal of Cell Biology
CODEN: JCLBA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Recent evidence from several laboratories shows that the paired helical filaments of %%%Alzheimer%%%'s disease brains consist mainly of the protein %%%tau%%% in an abnormally %%%phosphorylated%%% form, but the mode of assembly is not understood. Here we use EM to study several constructs derived from human brain %%%tau%%% and expressed in Escherichia coli. All constructs or %%%tau%%% isoforms are rodlike molecules with a high tendency to dimerize in an antiparallel fashion, as shown by antibody labeling and chemical crosslinking. The length of the rods is largely determined by the region of internal repeats that is also responsible for microtubule binding. One unit length of the repeat domain (three or four repeats) is around 22-25 nm, comparable to the cross-section of %%%Alzheimer%%% PHF cores. Constructs corresponding roughly to the repeat region of %%%tau%%% can form synthetic paired helical filaments resembling those from %%%Alzheimer%%% brain tissue. A similar self-assembly occurs with the chemically cross-linked dimers. In both cases there is no need for %%%phosphorylation%%% of the protein.

8/7/44 (Item 44 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08358377 BIOSIS NO.: 000094098900
THE %%%ALZHEIMER%%%-LIKE %%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEIN REDUCES
MICROTUBULE BINDING AND INVOLVES SER-PRO AND THR-PRO MOTIFS
AUTHOR: GUSTKE N; STEINER B; MANDELKOW E-M; BIERNAT J; MEYER H E; GOEDERT M
; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANCK-UNIT STRUCTURAL MOL. BIOL., C/O DESY,

NOTKESTRASSE 85, D-2000 HAMBURG 52, GERMANY.
JOURNAL: FEBS (FED EUR BIOCHEM SOC) LETT 307 (2). 1992. 199-205. %%%1992%%%
FULL JOURNAL NAME: FEBS (Federation of European Biochemical Societies)
Letters
CODEN: FEBLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% protein can be transformed into an %%%Alzheimer%%%-like state by %%%phosphorylation%%% with a kinase activity from brain [Biernat et al. (1992) EMBO J. 11, 1593-1597]. Here we show that the %%%phosphorylation%%% at Ser-Pro motifs strongly decreases %%%tau%%%'s affinity for microtubules. The major reduction occurs during the first of the three main stages of %%%phosphorylation%%%. The data explain the lower stability of microtubules resulting from the pathological %%%tau%%% %%%phosphorylation%%%.

8/7/45 (Item 45 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08336193 BIOSIS NO.: 000094087441
BRAIN LEVELS OF MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% ARE ELEVATED IN %%%ALZHEIMER%%%'S DISEASE A RADIOIMMUNO-SLOT-BLOT ASSAY FOR NANOGRAMS OF THE PROTEIN
AUTHOR: KHATOON S; GRUNDKE-IQBAL I; IQBAL K
AUTHOR ADDRESS: NEW YORK STATE INST. BASIC RES. DEVELOPMENTAL DISABILITIES, 1050 FOREST HILL RAOD, STATEN ISLAND N.Y. 10314.
JOURNAL: J NEUROCHEM 59 (2). 1992. 750-753. %%%1992%%%
FULL JOURNAL NAME: Journal of Neurochemistry
CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The microtubule-associated protein .%%%tau%%%., which stimulates the assembly of .alpha.-.beta. tubulin heterodimers into microtubules, is abnormally %%%phosphorylated%%% in %%%Alzheimer%%%'s disease (AD) brain and is the major component of paired helical filaments. In the present study, the levels of .%%%tau%%%. and abnormally %%%phosphorylated%%% . %%%tau%%%. were determined in brain homogenates of AD and age-matched control cases. A radioimmuno-slot-blot assay was developed, using a primary monoclonal antibody, %%%Tau%%%-1, and a secondary antibody, anti-mouse 125I-immunoglobulin G. To assay the abnormally %%%phosphorylated%%% .%%%tau%%%., the blots were treated with alkaline phosphatase before immunolabeling. The levels of total .%%%tau%%%. were about eightfold higher in AD (7.3 .+-. 2.7 ng/.mu.g of protein) than in control cases (0.9 .+-. 0.2 ng/.mu.g), and this increase was in the form of the abnormally %%%phosphorylated%%% protein. These studies indicate that the abnormal %%%phosphorylation%%% - not a decrease in the level of .%%%tau%%%. - is a likely cause of neurofibrillary degeneration in AD.

8/7/46 (Item 46 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08313834 BIOSIS NO.: 000094076157
EFFECTS OF MICROTUBULE STABILIZATION AND DESTABILIZATION ON %%%TAU%%% IMMUNOREACTIVITY IN CULTURED HIPPOCAMPAL NEURONS
AUTHOR: MATTSON M P
AUTHOR ADDRESS: 211 SANDERS-BROWN BUILDING, UNIV. KY., LEXINGTON, KY. 40536-0230, USA.
JOURNAL: BRAIN RES 582 (1). 1992. 107-118. %%%1992%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% immunoreactivity is altered in neurofibrillary tangles (NFT) and degenerating neurites in %%%Alzheimer%%%'s disease (AD). In addition, cytoskeletal proteins including %%%tau%%% are excessively %%%phosphorylated%%% in AD. Previous data indicated that calcium influx can cause antigenic changes in %%%tau%%% in cultured rat hippocampal and human cortical neurons similar to those seen in NFT. The present study used cultured hippocampal neurons to test the hypothesis that disruption of microtubules is a key event leading to altered antigenic properties of %%%tau%%% that result from calcium influx. As previously reported, we found that glutamate (100-500 .mu.M) and calcium ionophore A23187 (0.5-1 .mu.M) elevated intraneuronal calcium levels and caused a reduction in microtubules, a marked increase in staining with Alz-50 and 5E2, and a decrease in %%%tau%%%-1 immunoreactivity. The microtubule-disrupting agent colchicine (1 .mu.M) caused increased immunoreactivity of neurons towards %%%tau%%% antibodies Alz-50 and 5E2, and these effects of colchicine occurred in the absence of an increase in intracellular calcium levels. The microtubule-stabilizing drug taxol (100 nM) reduced neuronal immunoreactivity towards Alz-50 and 5E2 in untreated cultures and in cultures exposed to glutamate or A23187. Western blot analysis indicated that A23187 caused a reduction in %%%tau%%% levels which was partially prevented by taxol, suggesting that %%%tau%%% associated with microtubules is less susceptible to calcium-mediated degradation. Acid phosphatase treatment increased neuronal immunoreactivity towards %%%tau%%%-1 and reduced immunoreactivity towards Alz-50. The calcium-induced alterations in %%%tau%%% immunoreactivity were, and the colchicine-induced alterations were not, affected by acid phosphatase treatment. Taken together, the data indicate that microtubule depolymerization can cause antigen changes in %%%tau%%% similar to those seen in NFT independently of an increase in intraneuronal calcium levels. Stabilization of microtubules prevented the antigenic changes in %%%tau%%% suggesting that microtubules affect the availability and/or properties of epitopes on %%%tau%%% that are recognized by antibodies that stain NFT.

8/7/47 (Item 47 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08293779 BIOSIS NO.: 000094065077
%%%PHOSPHORYLATION%%%-DEPENDENT EPITOPES OF NEUROFILAMENT ANTIBODIES ON %%%TAU%%% PROTEIN AND RELATIONSHIP WITH %%%ALZHEIMER%%% %%%TAU%%%
AUTHOR: LICHTENBERG-KRAAG B; MANDELKOW E-M; BIERNAT J; STEINER B; SCHROETER C; GUSTKE N; MEYER H E; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANK-UNIT FOR STRUCTURAL MOLECULAR BIOL., C/O DESY, NOTKESTRASSE 85, D-2000 HAMBURG 52, WEST GERMANY.
JOURNAL: PROC NATL ACAD SCI U S A 89 (12). 1992. 5384-5388. %%%1992%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have studied the %%%phosphorylation%%% of

%%%tau%%% protein
from %%%Alzheimer%%% paired helical filaments, of %%%tau%%% from normal
human brain, and of recombinant %%%tau%%% isoforms. As a tool we used monoclonal antibodies against neurofilament protein that crossreact with %%%tau%%% in a %%%phosphorylation%%%-dependent manner. This allowed us to
deduce the state of %%%phosphorylation%%% in normal and pathological %%%tau%%%, as well as antibody epitopes. The epitope of antibody SMI33 is
at the first Lys-Ser-Pro sequence motif (residues 234-236) and requires an unphosphorylated Ser-235. Antibody SMI31 binds between Ser-396 (in the
second Lys-Ser-Pro motif) and Ser-404, both of which must be %%%phosphorylated%%%. SMI34 has a conformational epitope that depends on
the interaction between regions on either side of the microtubule-binding region; it also requires %%%phosphorylation%%%. The %%%phosphorylatable%%% serines detected by the SMI antibodies are part of
Ser-Pro motifs and can be %%%phosphorylated%%% by a protein kinase activity that can be used to induce a paired helical filament-like state in human brain %%%tau%%% in vitro. The phosphates are incorporated in several stages that can be identified by antibody reactivity and gel shift. This sguggests a role for the %%%phosphorylation%%% sites in %%%Alzheimer%%% disease, as well as the involvement of a Ser-Pro-directed
protein kinase.

8/7/48 (Item 48 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08272310 BIOSIS NO.: 000094053483
MITOGEN ACTIVATED PROTEIN MAP KINASE TRANSFORMS %%%TAU%%% PROTEIN INTO AN
%%%ALZHEIMER%%%-LIKE STATE
AUTHOR: DREWES G; LICHTENBERG-KRAAG B; DOERING F; MANDELKOW E-M; BIERNAT J;
GORIS J; DOREE M; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANCK-UNIT STRUCTURAL MOLECULAR BIOLOGY, C/O DESY,
NOTKESTRASSE 85, D-2000 HAMBURG 52, GER.
JOURNAL: EMBO (EUR MOL BIOL ORGAN) J 11 (6). 1992. 2131-2138. %%%1992%%%
FULL JOURNAL NAME: EMBO (European Molecular Biology Organization) Journal
CODEN: EMJOD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The microtubule-associated protein %%%tau%%% is a major component
of the paired helical filaments (PHFs) observed in %%%Alzheimer%%%'s disease brains. The pathological %%%tau%%% is distinguished from normal %%%tau%%% by its state of %%%phosphorylation%%%, higher apparent Mr and
reaction with certain antibodies. However, the protein kinase(s) have not been characterized so far. Here we describe a protein kinase from brain which specifically induces the %%%Alzheimer%%%-like state in %%%tau%%%
protein. The 42 kDa protein belongs to the family of mitogen activated protein kinases (MAPKs) and is activated by tyrosine %%%phosphorylation%%%. It is capable of %%%phosphorylating%%% Ser-Pro and
Thr-Pro motifs in %%%tau%%% protein (.apprxeq. 14-16 P1 per %%%tau%%%
molecule). By contrast, other proline directed Ser/Thr kinases such as p34(cdc2) combined with cyclin A or B have only minor effects on %%%tau%%% %%%phosphorylation%%%. We propose that MAP kinase is abnormally
active in %%%Alzheimer%%% brain tissue, or that the corresponding phosphatases are abnormally passive, due to a breakdown of the normal regulatory mechanisms.

8/7/49 (Item 49 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08230506 BIOSIS NO.: 000094031470
%%%TAU%%% PROTEIN KINASE I CONVERTS NORMAL %%%TAU%%% PROTEIN INTO A68-LIKE
COMPONENT OF PAIRED HELICAL FILAMENTS
AUTHOR: ISHIGURO K; TAKAMATSU M; TOMIZAWA K; OMORI A; TAKAHASHI M; ARIOKA M
; UCHIDA T; IMAHORI K
AUTHOR ADDRESS: MITSUBISHI KASEI INSTITUTE LIFE SCIENCES, 11 MINAMIOOYA,
MACHIDA-SHI, TOKYO 194, JPN.
JOURNAL: J BIOL CHEM 267 (15). 1992. 10897-10901. %%%1992%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: From bovine brain microtubules we purified %%%tau%%% protein
kinase I (TPKI, Mr 45,000 on sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE)) and %%%tau%%% protein kinase II (TPKII) whose
activity was attributed to a 30-kDa protein on SDS-PAGE by affinity-labeling using an ATP analog. Both kinases were activated by tubulin. TPKII, but not TPKI, %%%phosphorylated%%% %%%tau%%% fragment
peptides previously used for detection of a Ser/ThrPro kinase activity. Therefore, TPKII was considered to be the Ser/ThrPro kinase. TPKI was more effective than TPKII for producing the decrease of %%%tau%%%-1 immunoreactivity and mobility shift of %%%tau%%% on SDS-PAGE. Moreover,
TPKI, but not TPKII nor other well-known protein kinases, generated an epitope present on paired helical filaments. These findings suggested that %%%tau%%% %%%phosphorylated%%% by TPKI resembled A-68, a component
of paired helical filaments.

8/7/50 (Item 50 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08207577 BIOSIS NO.: 000094019850
WHAT'S NEW IN THE PATHOLOGY OF NEURONAL CYTOSKELETON THE SIGNIFICANCE OF
NEUROFIBRILLARY TANGLES
AUTHOR: DUSTIN P; BRION J-P; FLAMENT-DURAND J
AUTHOR ADDRESS: 808 ROUTE DE LENNIK, 1070-BRUSSELS, BELGIUM.
JOURNAL: PATHOL RES PRACT 188 (1-2). 1992. 248-253. %%%1992%%%
FULL JOURNAL NAME: Pathology Research and Practice
CODEN: PARPD
DOCUMENT TYPE: Review
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Neurofibrillary tangles are a neuronal change observed in various
conditions, linked with dementia when affecting the cerebral cortex as in %%%Alzheimer%%%'s disease. They may be found locally close to fibrous or
vascular tumors, or affect extensive regions of the neocortex while the cerebellum and the medulla are not affected. Recent immunological and biochemical studies demonstrate that the MT-associated protein %%%tau%%%
is the main component of the tangles, in an abnormally %%%phosphorylated%%% state. A consequence of the formation of tangles is
a decreased assembly of MT in axons and dendrites, with disturbances of neuroplasmic flow. The relations between tangles and amyloid, as seen in %%%Alzheimer%%%'s and Down's diseases are topographical, tangles accumulating in particular in neurites close to the amyloid in the senile plaques (but also at distance in cell bodies and neurites). Genetically and biochemically A4 or .beta.-amyloid and %%%tau%%% differ. The exact

relation between the .beta.-pleated proteins of tangles and amyloid remain poorly understood.

8/7/51 (Item 51 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08207529 BIOSIS NO.: 000094019802
FETAL-TYPE %%%PHOSPHORYLATION%%% OF THE %%%TAU%%% IN PAIRED HELICAL
FILAMENTS
AUTHOR: KANEMARU K; TAKIO K; MIURA R; TITANI K; IHARA Y
AUTHOR ADDRESS: DEP. NEUROPATHOLOGY, INSTITUTE BRAIN RESEARCH, FACULTY
MEDICINE, UNIVERSITY TOKYO, 7-3-1 HONGO, BUNKYO-KU, TOKYO 113, JPN.
JOURNAL: J NEUROCHEM 58 (5). 1992. 1667-1675. %%%1992%%%
FULL JOURNAL NAME: Journal of Neurochemistry
CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: To determine the %%%phosphorylation%%% sites of the .%%%tau%%%.
in paired helical filaments (PHF), two types of PHF antisera with different specificities were used: One was a conventional anti-PHF, and the other was an antiserum to formic acid-denatured PHF (anti-HFoPHF). %%%Phosphorylated%%% .%%%tau%%%.-specific antibodies, anti-ptau 1 and
anti-ptau 2, were prepared from anti-PHF and anti-HFoPHF, respectively. We found that both anti-ptau 1 and anti-ptau 2 labeled fetal or juvenile .%%%tau%%%. but not adult .%%%tau%%%.. The anti-ptau 1- and anti-ptau 2-recognition sites were immunochemically localized to the fragment Asp313 to Ile328 in the most COOH-terminal portion of .%%%tau%%%.. furthermore, Ser315 was determined as the anti-ptau 2 recognition site. The sequence surrounding Ser315 was not found in the canonical sequences %%%phosphorylated%%% with known kinases.

8/7/52 (Item 52 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08197761 BIOSIS NO.: 000043009234
ALZ50 RECOGNIZES A NON-%%%PHOSPHORYLATED%%% EPITOPE OF %%%TAU%%% IN NORMAL
AND %%%ALZHEIMER%%%'S DISEASE CEREBRAL CORTEX
AUTHOR: PARKINSON D; MCMANUS D Q; MORRIS J C
AUTHOR ADDRESS: DEP. CELL BIOLOGY, WASHINGTON UNIVERSITY MEDICAL SCHOOL,
ST. LOUIS, MO. 63110.
JOURNAL: KEYSTONE SYMPOSIUM ON ADVANCES IN UNDERSTANDING NEURODEGENERATIVE
DISORDERS, BIG SKY, MONTANA, USA, MARCH 28-APRIL 4, 1992. J CELL BIOCHEM
SUPPL 0 (16 PART E). 1992. 208. %%%1992%%%
CODEN: JCBSD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/53 (Item 53 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08183942 BIOSIS NO.: 000094007715
FAMILIAL %%%ALZHEIMER%%%'S DISEASE WITH THE AMYLOID PRECURSOR PROTEIN
POSITION 717 MUTATION AND SPORADIC %%%ALZHEIMER%%%'S DISEASE HAVE THE
SAME CYTOSKELETAL PATHOLOGY
AUTHOR: LANTOS P L; LUTHERT P J; HANGER D; ANDERTON B H; MULLAN M; ROSSOR M
AUTHOR ADDRESS: INST. PSYCHIATRY, DE CRESPIGNY PARK, LONDON SE5 8AF, UK.
JOURNAL: NEUROSCI LETT 137 (2). 1992. 221-224. %%%1992%%%
FULL JOURNAL NAME: Neuroscience Letters
CODEN: NELED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The cytoskeletal pathology of a patient with familial %%%Alzheimer%%%'s disease (AD) associated with the probably causal amyloid precursor protein (APP) codon 717 Val .fwdarw. Ile mutation is described. In addition to moderately extensive .beta.A4 protein deposition within the substance of the brain and in blood vessel walls (congophilic angiopathy), there was abundant cytoskeletal pathology in the form of neurofibrillary tangles, plaque neurites and neuropil threads. Interestingly, plentiful cortical and subcortical Lewy bodies were also seen. In order to compare the cytoskeletal pathology in this case with that seen in sporadic cases of AD we (1) studied the immunohistochemical profile of the amyloid and cytoskeletal pathology with antibodies to .beta.A4 protein, %%%tau%%%, %%%phosphorylated%%%
neurofilament epitopes and ubiquitin and (2) performed a bicohemical fractionation and Western blot analysis for the abnormally %%%phosphorylated%%% form of %%%tau%%% (A68) characteristically seen in
AD. No substantial difference between the familial case and sporadic cases could be found. We conclude that it is now reasonable to hypothesise that an abnormality in APP metabolism is responsible not only for the deposition of .beta.A4 protein, but also for the range of cytoskeletal pathology, typical of AD.

8/7/54 (Item 54 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08161385 BIOSIS NO.: 000093136833
IMMUNOLOGICAL CHARACTERIZATION OF THE REGION OF %%%TAU%%% PROTEIN THAT IS
BOUND TO %%%ALZHEIMER%%% PAIRED HELICAL FILAMENTS
AUTHOR: CAPUTO C B; WISCHIK C; NOVAK M; SCOTT C W; BRUNNER W F; DE GARCINI
E M; LO M M S; NORRIS T E; SALAMA A I
AUTHOR ADDRESS: ICI PHARMACEUTICALS GROUP, ICI AMERICAS, BMRL-2,
WILMINGTON, DEL. 19897.
JOURNAL: NEUROBIOL AGING 13 (2). 1992. 267-274. %%%1992%%%
FULL JOURNAL NAME: Neurobiology of Aging
CODEN: NEAGD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% protein in known to be present in the paired helical
filaments (PHFs) of %%%Alzheimer%%% brain. This study investigated the fragments of %%%tau%%% protein that remain bound to pronase-treated PHFs
and conditions that lead to the release of these %%%tau%%% fragments from
the core structure of the PHF. Antibody 423 reacted with PHFs and with fetal rat %%%tau%%% but not with adult rat %%%tau%%%, pig %%%tau%%%, or
recombinant human %%%tau%%%. Three other antibodies reacted with the tubulin binding region of %%%tau%%% only reacted with PHFs after they were disrupted with formic acid or guanidine. Other antibodies that recognize %%%tau%%% sequences C terminal to the tubulin binding region also recognized pronase-treated PHFs. Antibodies SM134 and T3P that recognize %%%phosphorylated%%% epitopes were reactive with pronase-treated PHFs. %%%Tau%%% fragments from the PHF were solubilized
by acid or guanidine treatment. These findings suggest that the fragments of %%%tau%%% that are bound to PHFs and protected from pronase digestion
include sequences from the tubulin binding region to the C terminus of %%%tau%%%. In addition, some of these sequences appear to be conformationally or post-translationally modified.

8/7/55 (Item 55 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08124334 BIOSIS NO.: 000042104957
ABNORMAL %%%PHOSPHORYLATION%%% OF %%%TAU%%% IS ONE OF THE EARLIEST EVENTS
IN %%%ALZHEIMER%%% NEUROFIBRILLARY PATHOLOGY
AUTHOR: KOPKE-SECUNDO E; GRUNDKE-IQBAL I; IQBAL K
AUTHOR ADDRESS: INST. BASIC RES. IN DEV. DISABILITIES, NEW YORK, N.Y.
10314.
JOURNAL: 21ST ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, NEW ORLEANS,
LOUISIANA, USA, NOVEMBER 10-15, 1991. SOC NEUROSCI ABSTR 17 (1-2). 1991.
1070. %%%1991%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/56 (Item 56 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08124329 BIOSIS NO.: 000042104952
%%%PHOSPHORYLATION%%% MODULATES DEGRADATION AND FUNCTION OF INDIVIDUAL
HUMAN %%%TAU%%% ISOFORMS
AUTHOR: LITERSKY J M; SCOTT C W; JOHNSON G V W
AUTHOR ADDRESS: DEP. PSYCHIATRY, UNIV. ALA., BIRMINGHAM, ALA. 35294.
JOURNAL: 21ST ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, NEW ORLEANS,
LOUISIANA, USA, NOVEMBER 10-15, 1991. SOC NEUROSCI ABSTR 17 (1-2). 1991.
1069. %%%1991%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/57 (Item 57 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08124328 BIOSIS NO.: 000042104951
%%%PHOSPHORYLATION%%% AND METABOLISM OF %%%TAU%%%
AUTHOR: JOHNSON G V W; LITERSKY J M
AUTHOR ADDRESS: DEP. PSYCHIATRY, UNIV. ALA., BIRMINGHAM, ALA. 35294.
JOURNAL: 21ST ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, NEW ORLEANS,
LOUISIANA, USA, NOVEMBER 10-15, 1991. SOC NEUROSCI ABSTR 17 (1-2). 1991.
1069. %%%1991%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/58 (Item 58 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08092284 BIOSIS NO.: 000093102357
REGIONS WITH ABUNDANT NEUROFIBRILLARY PATHOLOGY IN HUMAN BRAIN EXHIBIT A
SELECTIVE REDUCTION IN LEVELS OF BINDING-COMPETENT %%%TAU%%% AND
ACCUMULATION OF ABNORMAL %%%TAU%%%-ISOFORMS A68 PROTEINS
AUTHOR: BRAMBLETT G T; TROJANOWSKI J Q; LEE V M-Y
AUTHOR ADDRESS: MALONE BUILD. A009 HOSP. UNIV. PENNSYLVANIA, PHILADELPHIA,
PA. 19104-4283.
JOURNAL: LAB INVEST 66 (2). 1992. 212-222. %%%1992%%%
FULL JOURNAL NAME: Laboratory Investigation
CODEN: LAINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Paired helical filaments, the dominant filamentous components of
%%%Alzheimer%%%'s disease (AD), neurofibrillary tangles (NFT), neuropil threads, and the dystrophic neurites associated with amyloid rich sensile plaques, are composed of abnormally %%%phosphorylated%%% derivatives of .
%%%tau%%%. known as A68 proteins. Indeed the inappropriate phosphatorylation of Ser396, which is adjacent to the microtuble binding domain in .%%%tau%%%., may contribute to the transformation of .%%%tau%%%
. into A68 and prevent A68 from efficiently binding to microtubules. The reduced levels of normal soluble .%%%tau%%%. proteins in AD brains may be
the consequence of a multi-step process whereby normal .%%%tau%%%. is converted into A68 and sequestered in paired helical filaments. To elucidate the events involved in this process, we compared the relative levels of binding-competent (BC) and binding-incompetent (BI) .%%%tau%%%.
with the level of A68 in six different regions (hippocampus, fornix, frontal grey and white matter, and cerebellar grey and white matter) of fresh AD and control brains. When the AD brains were compared as a group
with neurologically normal and diseased non-AD controls, quantitative immunoblot analysis demonstrated a selective reduction of BC.%%%tau%%%.
in regions of the AD brains with abundant neurofibrillary lesions (NFTs, neuropil threads, and senile plaque neurites) and in their associated white matter areas. The level of BI.%%%tau%%%. was similar in both AD and
control brains. In contrast, A68 was present only in the AD brains, but it was confined to those brain regions with abundant NFTs, neuropil threads, and sensile plaques. We view the reductions in BC.%%%tau%%%. in fornix and frontal white matter to be a consequence of the reductions in their associated grey matter regions i.e., hippocampus and frontal grey matter. Although there is no strict relationship bewteen the reduction of BC.%%%tau%%%. and the level of A68 within an individual brain, the comparison of the AD group with the control group suggests that the grey matter of the affected regions may be the site for the conversion of BC. %%%tau%%%. into A68. Further, this process may occur rapidly or via pathways that do not involve BI.%%%tau%%%. since the levels of BI. %%%tau%%%. were similar in AD and control brains. Although the complete sequence of events leading to the transformation of .%%%tau%%%. into A68
and paired helical filaments remains to be elucidated, our data provide compelling evidence that A68 proteins are generated from .%%%tau%%% .-proteins in selected regions of the AD brain where neurofibrillary lesions comprised of paired helical filaments accumulate.

8/7/59 (Item 59 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08046217 BIOSIS NO.: 000093079565
REVERSIBLE BETA-PLEATED SHEET FORMATION OF A %%%PHOSPHORYLATED%%% SYNTHETIC
%%%TAU%%% PEPTIDE
AUTHOR: LANG E; SZENDREI G I; ELEKES I; LEE V M-Y; OTVOS L JR
AUTHOR ADDRESS: THE WISTAR INST. ANATOMY BIOL., 3601 SPRUCE STREET,
PHILADELPHIA, PA. 19104.
JOURNAL: BIOCHEM BIOPHYS RES COMMUN 182 (1). 1992. 63-69. %%%1992%%%
FULL JOURNAL NAME: Biochemical and Biophysical Research Communications
CODEN: BBRCA

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Serine416 of human .%%%tau%%%. protein is believed to be %%%phosphorylated%%% in %%%Alzheimer%%% neurofibrillary tangles. We synthesized a fragment of .%%%tau%%%., consisting of amino acids 408-421 in both non-%%%phosphorylated%%% and serine416-%%%phosphorylated%%% forms. Circular dichroism in a trifluoroethanol-water mixture indicated a .beta.-turn .fwdarw. .beta.-pleated sheet conformational transition upon %%%phosphorylation%%%. The .beta.-structure formation is intermolecular and can be inhibited by addition of Ca2+ ions or a %%%phosphorylated%%% tripeptide, but not with its non-%%%phosphorylated%%% analog. The presence of the %%%phosphorylated%%% .%%%tau%%%. peptide did not facilitate the formation of .beta.-pleated sheets of a %%%phosphorylated%%% neurofilament fragment. Multivalent cations induced a conformational transition of this %%%phosphorylated%%% neurofilament peptide, but the effect was less specific than the transition induced in the .%%%tau%%%. fragment, and it could also be reversed with the competing %%%phosphorylated%%% tripeptide.

8/7/60 (Item 60 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08042481 BIOSIS NO.: 000093075829
%%%PHOSPHORYLATION%%% BY CAMP-DEPENDENT PROTEIN KINASE INHIBITS THE DEGRADATION OF %%%TAU%%% BY CALPAIN
AUTHOR: LITERSKY J M; JOHNSON G V W
AUTHOR ADDRESS: SPARKS CENTER, ROOM 1011, UNIVERSITY ALABAMA BIRMINGHAM, BIRMINGHAM, ALA. 35294.
JOURNAL: J BIOL CHEM 267 (3). 1992. 1563-1568. %%%1992%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effects of cAMP-dependent protein kinase (cAMP-PK) %%%phosphorylation%%% on the degradation of the microtubule-associated protein %%%tau%%% by calpain were studied. Purified bovine brain %%%tau%%% that had been %%%phosphorylated%%% by cAMP-PK had a slower migration pattern on sodium dodecyl sulfate-polyacrylamide gels and a more acidic, less heterogenous pattern on two-dimensional, nonequilibrium pH gradient electrophoresis (NEPHGE) gels compared with untreated %%%tau%%%. %%%Phosphorylation%%% of %%%tau%%% by cAMP-PK significantly inhibited its proteolysis by calpain compared with untreated %%%tau%%%. To our knowledge this is the first demonstration that %%%phosphorylation%%% of %%%tau%%% by a specific kinase results in increased resistance to hydrolysis by calpain. %%%Tau%%% dephosphorylated by alkaline phosphatase migrated more rapidly on sodium dodecyl sulfate-polycrylamide gels and also showed an altered two-dimensional NEPHGE pattern. Dephosphorylation of %%%tau%%% had no effect on its susceptibility to calpain proteolysis, indicating that regulation of the susceptibility to calpain hydrolysis is due to the %%%phosphorylation%%% of a specific site(s). These results suggest a role for %%%phosphorylation%%% in regulating the degradation of %%%tau%%%. Abnormal %%%phosphorylation%%% could result in a protease-resistant %%%tau%%% population which may contribute to the formation of pired helical filaments in %%%Alzheimer%%%'s disease.

8/7/61 (Item 61 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

08035663 BIOSIS NO.: 000042062486
PAIRED HELICAL FILAMENTS PHF AND ABNORMALLY %%%PHOSPHORYLATED%%% %%%TAU%%%
AUTHOR: IHARA Y; HASEGAWA M; MORISHIMA M; TAKIO K
AUTHOR ADDRESS: DEP. NEUROPATHOL., INST. BRAIN RES., UNIV. TOKYO, 7-3-1 HONGO, BUNKYO-KU, TOKYO 113, JPN.
JOURNAL: THE FIFTEENTH ANNUAL MEETING OF THE JAPAN NEUROSCIENCE SOCIETY, TOKYO, JAPAN, DECEMBER 17-19, 1991. NEUROSCI RES SUPPL 0 (16). 1991. VIII. %%%1991%%%
CODEN: NRSUE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/62 (Item 62 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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08022634 BIOSIS NO.: 000093067557
IN-SITU HYBRIDIZATION OF CALCIUM-CALMODULIN DEPENDENT PROTEIN KINASE II AND %%%TAU%%% MRNAS SPECIES DIFFERENCES AND RELATIVE PRESERVATION IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: MAH V H; ESKIN T A; KAZEE A M; LAPHAM L; HIGGINS G A
AUTHOR ADDRESS: THOMAS JEFFERSON UNIV., DIV. NEUROPATHOL., 130 SOUTH 9TH ST., SUITE 400, PHILADELPHIA, PA. 19107, USA.
JOURNAL: MOL BRAIN RES 12 (1-3). 1992. 85-94. %%%1992%%%
FULL JOURNAL NAME: Molecular Brain Research
CODEN: MBREE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Abnormal %%%phosphorylation%%% of the microtubule associated protein %%%tau%%% component of neurofibrillary tangles (NFTs) in %%%Alzheimer%%%'s disease (AD) may result from alterations in protein kinase expression. Calcium/calmodulin dependent protein kinase II (CaM kinase II) has been shown to %%%phosphorylate%%% %%%tau%%% in vitro in such a way to decrease its electrophoretic mobility. A68, apparently a modified form of %%%tau%%% in AD brain, also shows abnormal %%%phosphorylation%%% and slower mobility than %%%tau%%%. To further examine the role of CaM kinase II in AD, in situ hydridization studies were performed on tissues from rat, monkey and human to examine and compare the patterns of CaM kinase II mRNA expression in different brain regions. The most notable differences among the three species were observed in dendrites in layer I of isocortex, in the molecular layer of the dentate gyrus and stratum radiatum and stratum lacunosum-moleculare in hippocampus, where hybridization was detected in rat, but not in monkey or human brain. In addition, comparisons between %%%tau%%% and CaM kinase II mRNA expression were made in tissue from normal aged adults and AD patients, especially in areas prone to NFT formation. CaM kinase II and %%%tau%%% mRNAs were co-expressed in many neuronal populations, both those which are prone to NFT formation as well as those which are rarely affected by AD changes. No major differences in the relative abundance of either CaM kinase II or %%%tau%%% mRNA within particular neuronal populations was noted between normal aged and AD brain. Diminished hybridization was associated with severe neuronal pathology and cell loss.

8/7/63 (Item 63 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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07999668 BIOSIS NO.: 000093055341

EFFECTS OF ELEVATED INTRACELLULAR CALCIUM LEVELS ON THE CYTOSKELETON AND
%%%TAU%%% IN CULTURED HUMAN CORTICAL NEURONS
AUTHOR: MATTSON M P; ENGLE M G; RYCHLIK B
AUTHOR ADDRESS: SANDERS-BROWN RES. CENT. AGING, DEP. ANATOMY NEUROBIOL.,
UNIV. KENTUCKY MED. CENT., LEXINGTON, KY. 40536-0230.
JOURNAL: MOL CHEM NEUROPATHOL 15 (2). 1991. 117-142. %%%1991%%%
FULL JOURNAL NAME: Molecular and Chemical Neuropathology
CODEN: MCHNE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Considerable evidence suggests that altered neuronal calcium homeostasis plays a role in the neuronal degeneration that occurs in an array of neurological disorders. A reduction in microtubules, the accumulation of 8-15 nm straight filaments, and altered antigenicity toward antibodies to the microtubule-associated protein %%%tau%%% and ubiquitin, as well as granulovacuolar degeneration, are observed in many human neurodegenerative disorders. Progress towards understanding how and
why human neurons degenerate has been hindered by the inability to examine living human neurons under controlled conditions. We used cultured human fetal cerebral cortical neurons to examine ultrastructural and antigenic changes resulting from elevations in intracellular calcium levels. Elevation of intracellular calcium by exposure to a calcium ionophore or a reduced level of extracellular Na+ for period of hours to days caused a loss of microtubules, an increase in 8-15 nm straight filaments, and increased immunostaining with Alz-50 and 5E2 (%%%tau%%%
antibodies) and ubiquitin antibodies. Granulovacuolar degeneration was also observed. Antigenic changes in %%%tau%%% were sensitive to phosphatases, and the electrophoretic mobility of %%%tau%%% was altered
in cells exposed to calcium ionophore, indicating that %%%tau%%% was excessively %%%phosphorylated%%% as the result of elevated intracellular
calcium levels. Colchicine also caused an accumulation of straight filaments and altered %%%tau%%% immunoreactivity, suggesting that a disruption of microtubules secondary to altered calcium homeostasis may be a key event leading to altered %%%tau%%% disposition and neuronal degeneration. These data demonstrate that aberrant rises in intraneuronal calcium levels can result in changes in the neuronal cytoskeleton similar to those seen in neurodegenerative disorders, and suggest that this experimental system will be useful in furthering our understanding of the cellular and molecular mechanisms of human neurological disorders.

8/7/64 (Item 64 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07992890 BIOSIS NO.: 000093048563
HYDROFLUORIC ACID-TREATED %%%TAU%%%-PHF PROTEINS DISPLAY THE SAME
BIOCHEMICAL PROPERTIES AS NORMAL %%%TAU%%%
AUTHOR: GREENBERG S G; DAVIES P; SCHEIN J D; BINDER L I
AUTHOR ADDRESS: DEMENTIA RES., W. M. BURKE MED. RES. INST., 785 MAMARONECK
AVE., WHITE PLAINS, N.Y. 10605.
JOURNAL: J BIOL CHEM 267 (1). 1992. 564-569. %%%1992%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% (.%%%tau%%%.) is a major constituent of paired helical
filaments (PHF) found in %%%Alzheimer%%%'s disease. The current study examines the possibility that the distinct properties of PHF-associated . %%%tau%%%. proteins (.%%%tau%%%.PHF) result from post-translational modifications of normal soluble .%%%tau%%%. (.%%%tau%%%.s). Following hydrofluoric acid (HF) treatment, .%%%tau%%%.PHF proteins are heat- and
acid-stable, soluble in 2-(N-morpholino)ethanesulfonic acid buffers and display the same molecular weight, pI, and immunochemical properties as normal .%%%tau%%%.s. Alkaline phosphatase treatment of dissociated PHF results in similar, although less extensive, electrophoretic changes and a reduction in PHF-1 immunoreactivity. Therefore, %%%phosphorylation%%%
of normal .%%%tau%%%.s appears to be responsible for the distinct properties of .%%%tau%%%.PHF. Although our results suggest that all of the normal .%%%tau%%%. isoforms are in PHF, the relative abundance of individual .%%%tau%%%. species differs in HF-treated PHF and .%%%tau%%%.s
samples. Moreover, the loss of PHF following HF treatment suggests that post-translational modifications contribute to the structural stability of PHF.

8/7/65 (Item 65 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07989835 BIOSIS NO.: 000042041233
OKADAIC ACID PRODUCES DOSE-DEPENDENT NEUROTOXIC LESIONS AND INCREASED
%%%PHOSPHORYLATION%%% OF NEUROFILAMENT AND %%%TAU%%% PROTEINS IN-VIVO
AUTHOR: KOWALL N W; BEAL M F; MCKEE A C; KOSIK K S
AUTHOR ADDRESS: DEP. NEUROL., HARVARD MED. SCH., BOSTON, MASS. 02114.
JOURNAL: ABSTRACTS OF PAPERS PRESENTED AT THE THIRTY-FIRST ANNUAL MEETING
OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, BOSTON, MASSACHUSETTS, USA,
DECEMBER 8-12, 1991. J CELL BIOL 115 (3 PART 2). 1991. 385A. %%%1991%%%
CODEN: JCLBA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/66 (Item 66 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07989834 BIOSIS NO.: 000042041232
%%%ALZHEIMER%%%-TYPE %%%PHOSPHORYLATION%%% OF MICROTUBLE-ASSOCIATED PROTEIN
%%%TAU%%% IN-VITRO
AUTHOR: LICHTENBERG-KRAAG B; STEINER B; MANDELKOW E-M; BIERNAT J; SCHROETER
C; MEYER H; GOEDERT M; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANCK-UNIT STRUCTURAL MOL. BIOL., HAMBURG, GERMANY.
JOURNAL: ABSTRACTS OF PAPERS PRESENTED AT THE THIRTY-FIRST ANNUAL MEETING
OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, BOSTON, MASSACHUSETTS, USA,
DECEMBER 8-12, 1991. J CELL BIOL 115 (3 PART 2). 1991. 384A. %%%1991%%%
CODEN: JCLBA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/67 (Item 67 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07989831 BIOSIS NO.: 000042041229
CHARACTERIZATION OF DIMERIC FORMS OF THE MICROTUBLE ASSOCIATED PROTEIN
%%%TAU%%%
AUTHOR: WILSON D M; VOELKER H M; BINDER L I
AUTHOR ADDRESS: DEP. CELL BIOL., UNIV. ALA., BIRMINGHAM, ALA. 35294.
JOURNAL: ABSTRACTS OF PAPERS PRESENTED AT THE THIRTY-FIRST

ANNUAL MEETING
OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, BOSTON, MASSACHUSETTS, USA,
DECEMBER 8-12, 1991. J CELL BIOL 115 (3 PART 2). 1991. 384A. %%%1991%%%
CODEN: JCLBA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/68 (Item 68 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07976309 BIOSIS NO.: 000093043887
BRAIN UBIQUITIN IS MARKEDLY ELEVATED IN %%%ALZHEIMER%%% DISEASE
AUTHOR: WANG G P; KHATOON S; IQBAL K; GRUNDKE-IQBAL I
AUTHOR ADDRESS: NEW YORK STATE INST., BASIC RES. DEV. DISABILITIES, 1050
FOREST HILL RD., STATEN ISLAND, N.Y. 10314.
JOURNAL: BRAIN RES 566 (1-2). 1991. 146-151. %%%1991%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Levels of ubiquitin, microtubule associated protein %%%tau%%% and tubulin were determined by immunoassays in homogenates of cerebrum and cerebellum of %%%Alzheimer%%% disease and aged control cases. Ubiquitin levels increased many fold in the cerebral cortex of %%%Alzheimer%%% disease cases and the increase correlated strongly with the degree of neurofibrillary changes in the tissue. The increase in ubiquitin was much less remarkable in the cerebral white matter. Cerebellum which is unaffected with neurofibrillary changes in %%%Alzheimer%%% disease had normal levels of ubiquitin both in gray matter and in white matter. There was an appreciable increase in abnormally %%%phosphorylated%%% %%%tau%%% in an %%%Alzheimer%%% disease brain with severe neurofibrillary degeneration, whereas the normal %%%tau%%% levels were increased only slightly. Tubulin was slightly decreased in the cerebral gray matter but not in the adjacent white matter. Marked increase in brain ubiquitin in %%%Alzheimer%%% disease suggests the role of ubiquitin in the pathobiology of %%%Alzheimer%%% disease.

8/7/69 (Item 69 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07952647 BIOSIS NO.: 000093031745
TWO NOVEL KINASES %%%PHOSPHORYLATE%%% %%%TAU%%% AND THE KSP SITE OF HEAVY NEUROFILAMENT SUBUNITS IN HIGH STOICHIOMETRIC RATIOS
AUTHOR: RODER H M; INGRAM V M
AUTHOR ADDRESS: ROOM 56-601, DEP. BIOL., MASS. INST. TECHNOL., CAMBRIDGE, MASS. 02139.
JOURNAL: J NEUROSCI 11 (11). 1991. 3325-3343. %%%1991%%%
FULL JOURNAL NAME: Journal of Neuroscience
CODEN: JNRSD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have identified, purified, and characterized two neurofilament/%%%tau%%% kinases from bovine brain, PK36 and PK40, with apparent Mr of 36,000 and 40,000 and with novel biochemical properties. A specially designed immunoassay for %%%phosphorylated%%% epitopes in neurofilament (NF) proteins was used in the early stages of the purification. Neither kinase is closely associated with the cytoskeleton. Both kinases %%%phosphorylate%%% bovine intermediate (NF-M) and heavy (NF-H) NF subunits and also bovine %%%tau%%% at the expected KSP sequences, though other sites cannot be ruled out. In human paired helical filaments, %%%tau%%%, %%%phosphorylated%%% at these same KSP sites, is a major characterized constituent. Neither kinase is activated by the usual second messengers. %%%Tau%%% and the above NF subunits are %%%phosphorylated%%% in high stoichiometric ratios. In the intermediate NF subunit, all the expected sites appear to be %%%phosphorylated%%%, but in the heavy NF subunit only 7 out of the > 40 expected sites can be %%%phosphorylated%%% by our kinases. We demonstrate that both kinases can induce considerable shifts of apparent Mr with SDS-PAGE for %%%tau%%% and, for the first time in vitro, also for the intermediate NF subunit. Interestingly, PK36 and particularly PK40 are strongly inhibited by an excess of free ATP. We proposed that during normal aging, and in %%%Alzheimer%%%'s disease, age-related mitochondrial dysfunction would reduce ATP levels, which in turn might release the neurofilament/ %%%tau%%% kinase from inhibition with consequent paired helical filament formation.

8/7/70 (Item 70 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07952374 BIOSIS NO.: 000093031472
ABNORMAL %%%TAU%%% PROTEINS FROM %%%ALZHEIMER%%%'S DISEASE BRAINS
PURIFICATION AND AMINO ACID ANALYSIS
AUTHOR: LIU W-K; KSIEZAK-REDING H; YEN S-H
AUTHOR ADDRESS: DEP. PATHOLOGY, F-538 ALBERT EINSTEIN COLLEGE MEDICINE, 1300 MORRIS PARK AVE., BRONX, N.Y. 10461.
JOURNAL: J BIOL CHEM 266 (32). 1991. 21723-21727. %%%1991%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Abnormal %%%tau%%% proteins (PHF-%%%tau%%%) were isolated form %%%Alzheimer%%%'s disease brains by treatment of paired helical filament enriched-fractions with perchloric acid and boiling of the acid precipitable fraction with .beta.-mercaptoethanol. These proteins were purified further by a second perchloric acid treatment. The purified PHF-%%%tau%%% proteins were soluble in buffers devoid of sodium dodecyl sulfate. However, they were similar to the abnormal %%%tau%%% extracted from paired helical filaments with sodium dodecyl sulfate, also named A68, in molecular mass (68, 64, and 60 kDa), isoelectric point (pI 5.5-6.5), reactivity with anti-%%%tau%%% antibodies, and in requirement for alkaline phosphatase treatment to bind the %%%Tau%%%-1 antibody. Compared to normal %%%tau%%%, the soluble PHF-%%%tau%%% contained 100% more glycine and 35% less lysine residue. The results suggest that besides %%%phosphorylation%%% other types of modification may be involved in differentiating PHF-%%%tau%%% from normal %%%tau%%%.

8/7/71 (Item 71 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07944599 BIOSIS NO.: 000042019872
POST-TRANSLATIONAL MODIFICATIONS OF A %%%TAU%%%-RELATED PROTEIN PRESENT IN PAIRED HELICAL FILAMENTS
AUTHOR: CORREAS I; DIAZ-NIDO J; AVILA J

AUTHOR ADDRESS: CENTRO BIOL. MOL., UNIV. AUTONOMA, CANTOBLANCO, 28049
MADRID, SPAIN.
JOURNAL: IQBAL, K., ET AL. (ED.). ALZHEIMER'S DISEASE: BASIC MECHANISMS,
DIAGNOSIS AND THERAPEUTIC STRATEGIES; SELECTED PAPERS FROM THE SECOND
INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED DISORDERS,
TORONTO, ONTARIO, CANADA, JULY 15-20, 1990. XV+675P. JOHN WILEY AND SONS,
INC.: NEW YORK, NEW YORK, USA; CHICHESTER, ENGLAND, UK. ILLUS. MAPS. ISBN
0-471-92927-1. 0 (0). 1991. 199-206. %%%1991%%%
CODEN: 35361
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/72 (Item 72 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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07931468 BIOSIS NO.: 000093019866
A68 PROTEINS IN %%%ALZHEIMER%%%'S DISEASE ARE COMPOSED OF SEVERAL %%%TAU%%%
ISOFORMS IN A %%%PHOSPHORYLATED%%% STATE WHICH AFFECTS THEIR
ELECTROPHORETIC MOBILITIES
AUTHOR: BRION J-P; HANGER D P; COUCK A-M; ANDERTON B H
AUTHOR ADDRESS: LAB. PATHOL. ELECTRON MICROSCOPY, UNIV. LIBRE DE BRUXELLES,
808 ROUTE DE LENNIK, BUILDING C-10, 1070 BRUSSELS, BELG.
JOURNAL: BIOCHEM J 279 (3). 1991. 831-836. %%%1991%%%
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The %%%tau%%%-immunoreactive A68 polypeptides found in brains
from patients with %%%Alzheimer%%%'s disease have been studied by Western
blotting using antibodies to synthetic peptides corresponding to
sequences that span the complete human %%%tau%%% molecule, and antibodies
specific for inserts 1 and 2 found towards the N-terminus of some
%%%tau%%% isoforms. The three major A68 polypeptides were labelled by all
of the antibodies to sequences common to all %%%tau%%% isoforms, but the
faster-migrating A68 polypeptide was not labelled by either of the two
antibodies specific for inserts 1 and 2. Treatment with alkaline
phosphatase of non-solubilized A68 did not change its electrophoretic
mobility on SDS/PAGE under the conditions described here. However, A68
that was solubilized before treating it with alkaline phosphatase was
found to move faster on SDS/PAGE than untreated A68, to a position
similar to that of normal %%%tau%%%. We also confirmed that A68
preparations contain numerous paired helical filaments (PHF). These PHF
were labelled by all anti-%%%tau%%% antibodies, including insert-specific
antibodies. Our results further support the notion that PHF contain
abnormally %%%phosphorylated%%% %%%tau%%% in an aggregated state, and
indicate that these abnormally %%%phosphorylated%%% %%%tau%%% forms are
composed of several %%%tau%%% isoforms and that the full length of the
%%%tau%%% molecule is present in these proteins.

8/7/73 (Item 73 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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07889611 BIOSIS NO.: 000092138901
EFFECTS OF INJECTED %%%ALZHEIMER%%% BETA AMYLOID CORES IN RAT BRAIN
AUTHOR: FRAUTSCHY S A; BAIRD A; COLE G M
AUTHOR ADDRESS: DEP. MOL. CELLULAR GROWTH BIOL., WHITIER INST. DIABETICS
ENDOCRINOL., 9894 GENESEE, LA JOLLA, CALIF. 92037.
JOURNAL: PROC NATL ACAD SCI U S A 88 (19). 1991. 8362-8366. %%%1991%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the
United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Although amyloid deposits have long been known to accumulate in
%%%Alzheimer%%% disease (AD) brain, their origin and significance remain
speculative. Because of the lack of an in vivo model where amyloid
deposits can be induced, the relationship of the extracellular
.beta.-amyloid deposits to another AD pathology has never been directly
investigated. Therefore, we injected SDS-isolated amyloid cores into rat
cortex and hippocampus. Similarly isolated lipofuscin fractions from
control human brains were injected on the contralateral side. Rats were
perfused and brains were examined immunohistochemically at 2 days, 7
days, and 1 month after injection. Alz-50, a monoclonal antibody against
abnormally %%%phosphorylated%%% %%%tau%%% proteins, stained neurons along
the cortical needle track at 2 but not 7 days after injection of either
amyloid or lipofuscin. At 1 month, however, ubiquitin, Alz-50 antigen,
and silver-positive structures were observed only in response to amyloid.
In 7 of 10 animals, there was considerable neuronal loss in the
hippocampal layers. In each instance, these effects were in the immediate
vicinity of .beta.-protein immunoreactive material. Marked neuronal loss
was never observed at any time after lipofuscin injection. These results
indicate a neuronal response to amyloid. When preparations of mature
plaque amyloid isolated from the AD brain are injected into the rat
brain, they exert neurotoxic effects and induce antigen found in the AD
brain.

8/7/74 (Item 74 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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07887023 BIOSIS NO.: 000092136024
AMYLOID DEPOSITION AS THE CENTRAL EVENT IN THE ETIOLOGY OF %%%ALZHEIMER%%%
'S DISEASE
AUTHOR: HARDY J; ALLSOP D
AUTHOR ADDRESS: DEP. BIOCHEM. AND MOLECULAR GENETICS, ST. MARY'S HOSP. MED.
SCH., LONDON W2 1PG, UK.
JOURNAL: TRENDS PHARMACOL SCI 12 (10). 1991. 383-388. %%%1991%%%
FULL JOURNAL NAME: Trends in Pharmacological Sciences
CODEN: TPHSD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: While there may be many causes of %%%Alzheimer%%%'s disease (AD),
the same pathological sequence of events, described here by John Hardy
and David Allsop, is likely to occur in all cases. The recent discovery
of a pathogenic mutation in the .beta.-amyloid precursor protein (APP)
gene on chromosome 21 suggests that APP mismetabolism and .beta.-amyloid
deposition are the primary events in the disease process. The occurrence
of AD in Down syndrome is consistent with this hypothesis. The
pathological cascade for the disease process is most likely to be:
.beta.-amyloid deposition .fwdarw. %%%tau%%% %%%phosphorylation%%% and
tangle formation .fwdarw. neuronal death. The development of a
biochemical understanding of this pathological cascade will facilitate
rational design of drugs to intervene in this process.

8/7/75 (Item 75 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07854389 BIOSIS NO.: 000041104010
%%%ALZHEIMER%%% DISEASE IN-VITRO DEPHOSPHORYLATION OF ABNORMALLY
%%%PHOSPHORYLATED%%% %%%TAU%%%
AUTHOR: IQBAL K; GRUNDKE-IQBAL I
AUTHOR ADDRESS: INST. BASIC RES., STATEN ISLAND, N.Y. 10314.
JOURNAL: THIRTEENTH MEETING OF THE INTERNATIONAL SOCIETY FOR
NEUROCHEMISTRY, SYDNEY, NEW SOUTH WALES, AUSTRALIA, JULY 15-19, 1991. J
NEUROCHEM 57 (SUPPL.). 1991. S111. %%%1991%%%
CODEN: JONRA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/76 (Item 76 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07844699 BIOSIS NO.: 000092114865
SENILE PLAQUE NEURITES IN %%%ALZHEIMER%%% DISEASE ACCUMULATE AMYLOID
PRECURSOR PROTEIN
AUTHOR: CRAS P; KAWAI M; LOWERY D; GONZALEZ-DEWHITT P; GREENBERG B; PERRY G
AUTHOR ADDRESS: INST. PATHOL., CASE WESTERN RESERVE UNIVERSITY, 2085
ADELBERT RD., CLEVELAND, OHIO 44106.
JOURNAL: PROC NATL ACAD SCI U S A 88 (17). 1991. 7552-7556. %%%1991%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the
United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Senile plaques are polymorphous .beta.-amyloid protein deposits found in the brain in Alzeheimer disease and normal aging. This .beta.-amyloid protein is derived from a larger precursor molecule of which neurons are the principal producers in brain. We found that amyloid precursor protein (APP)-immunoreactive neurites were involved in senile plaques and that only a subset of these neurites showed markers for the abnormal filaments characteristic of neurofibrillary pathology. In the neocortex of nondemented individuals with senile plaques but spared of neurofibrillary pathology, dystrophic neurites in senile plaques showed only APP accumulation. In contrast, in the brains of Alzeheimer patients, virtually all APP-immunoreactive neurites also showed immunoreactivity with ubiquitin, .%%%tau%%%., and %%%phosphorylated%%% neurofilaments. The
presence of .%%%tau%%%. and neurofilament epitopes in dystrophic neurites
in senile plaques was correlated with the extent of neurofibrillary pathology in the surrounding brain tissue. Accumulation of APP and the formation of neurofibrillary pathology in senile plaque neurites are therefore distinct phenomena. Our findings suggest that APP accumulation in senile plaque neurites occurs prior to .%%%tau%%%. accumulation and is therefore more closely related to appearance of neuritic dystrophy.

8/7/77 (Item 77 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07835361 BIOSIS NO.: 000041097527
%%%PHOSPHORYLATION%%% OF %%%TAU%%% IN TRANSFECTED NON-NEURONAL CELLS
AUTHOR: GALLO J-M; KOSIK K S; ANDERTON B H
AUTHOR ADDRESS: INST. PSYCHIATRY, LONDON SE5 8AF, UK.
JOURNAL: EIGHTY-FIRST MEETING OF THE BRITISH NEUROPATHOLOGICAL SOCIETY,
LONDON, ENGLAND, UK, JANUARY 10-11, 1991. NEUROPATHOL APPL NEUROBIOL 17
(3). 1991. 239. %%%1991%%%
CODEN: NANED
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/78 (Item 78 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07835360 BIOSIS NO.: 000041097526
ABNORMAL %%%TAU%%% PROTEIN IN %%%ALZHEIMER%%%'S DISEASE AND DOWN'S SYNDROME
IS INSOLUBLE AND IS %%%PHOSPHORYLATED%%% DIFFERENTLY FROM SOLUBLE
%%%TAU%%%
AUTHOR: HANGER D P; BRION J-P; CAIRNS N; LUTHERT P; ANDERTON B H
AUTHOR ADDRESS: INST. PSYCHIATRY, LONDON SE5 8AF, UK.
JOURNAL: EIGHTY-FIRST MEETING OF THE BRITISH NEUROPATHOLOGICAL SOCIETY,
LONDON, ENGLAND, UK, JANUARY 10-11, 1991. NEUROPATHOL APPL NEUROBIOL 17
(3). 1991. 239. %%%1991%%%
CODEN: NANED
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/79 (Item 79 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07797833 BIOSIS NO.: 000092090404
A SERINE-THREONINE PROLINE KINASE ACTIVITY IS INCLUDED IN THE %%%TAU%%%
PROTEIN KINASE FRACTION FORMING A PAIRED HELICAL FILAMENT EPITOPE
AUTHOR: ISHIGURO K; OMORI A; SATO K; TOMIZAWA K; IMAHORI K; UCHIDA T
AUTHOR ADDRESS: MITSUBISHI KASEI INSTITUTE LIFE SCIENCES, MINAMIOOYA 11,
MACHIDA-SHI, TOKYO, JPN. 194.
JOURNAL: NEUROSCI LETT 128 (2). 1991. 195-198. %%%1991%%%
FULL JOURNAL NAME: Neuroscience Letters
CODEN: NELED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Previously we partially purified a novel protein kinase which %%%phosphorylated%%% %%%tau%%% and formed a paired helical filament (PHF)
epitope. In this paper we show that the kinase fraction contains a protein kinase activity recognizing serine/threonine proline sequence. The kinase %%%phosphorylated%%% %%%tau%%% at the %%%tau%%%-1 site
previously reported as one of the %%%phosphorylation%%% sites on PHF by
others groups. The kinase also %%%phosphorylated%%% extraordinarily insoluble portion located on C-terminal region on %%%tau%%% in PHF. It is worth considering that %%%tau%%% %%%phosphorylated%%% by this kinase
activity is incorporated into PHF.

8/7/80 (Item 80 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07753150 BIOSIS NO.: 000092066871
ABNORMAL %%%TAU%%% PROTEINS IN PROGRESSIVE

SUPRANUCLEAR PALSY SIMILARITIES
AND DIFFERENCES WITH THE NEUROFIBRILLARY DEGENERATION OF THE
%%%ALZHEIMER%%% TYPE
AUTHOR: FLAMENT S; DELACOURTE A; VERNY M; HAUW J-J; JAVOY-AGID F
AUTHOR ADDRESS: UNITE INSERM 156, PLACE DE VERDUN, F-59045 LILLE, FR.
JOURNAL: ACTA NEUROPATHOL 81 (6). 1991. 591-596. %%%1991%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have previously shown that abnormal %%%Tau%%% species are
produced during the neurofibrillary degeneration of the %%%Alzheimer%%%
type. These abnormal %%%Tau%%% proteins consist of a characteristic
triplet named %%%Tau%%% 55, %%%Tau%%% 64 and %%%Tau%%% 69 which are
constantly found in %%%Alzheimer%%%'s disease (AD) and Downs syndrome
brain regions with tangles. To determine if abnormal %%%Tau%%% species
are also produced in other neurodegenerative conditions where
intraneuronal filamentous %%%Tau%%% aggregates are observed, we have
undertaken an immuno-blot study of brain homogenates from patients with
progressive supranuclear palsy (PSP), a neurological disorder
characterized by the presence of tangles in subcortical and cortical
brain areas. We show here that abnormal %%%Tau%%% species are produced in
PSP but that they are different from those in AD. Indeed, although
%%%Tau%%% 64 and 69 were present in PSP brain homogenates, possibly as
the result of an abnormal %%%phosphorylation%%% as in AD, they were
detected in smaller amounts (three times lower) than in AD. In addition
%%%Tau%%% 55 was undetected by the immunological tools, such as the
absorbed anti-PHF antisera, which specifically label the abnormal
%%%Tau%%% proteins. Also the two-dimensional analysis revealed different
isoelectric properties. Our results suggests that the production of
abnormal %%%Tau%%% species is a very important event during all types of
neurofibrillary degeneration. The differences in the pathological
%%%Tau%%%-variant profiles that were observed between PSP and AD possibly
reflect different etiopathogenetic pathways and might explain the
formation of different types filamentous %%%Tau%%% aggregates.

8/7/81 (Item 81 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07750535 BIOSIS NO.: 000092064256
EVIDENCE FOR %%%TAU%%% EXPRESSION IN CELLS OF MONOCYTE LINEAGE AND ITS
IN-VITRO %%%PHOSPHORYLATION%%% BY V-FMS KINASE
AUTHOR: KIM H; STRONG T V; ANDERSON S J
AUTHOR ADDRESS: UNIV. ALABAMA BIRMINGHAM, DEP. PATHOL., VOLKER HALL G-023,
UAB STATION, BIRMINGHAM, ALA. 35294, USA.
JOURNAL: ONCOGENE 6 (6). 1991. 1085-1088. %%%1991%%%
FULL JOURNAL NAME: Oncogene
CODEN: ONCNE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The v-fms encoded kinase, which is known to associate with
cytoskeletal elements, was shown to %%%phosphorylate%%% histiocytic
proteins that had physical and immunological attributes in common with
%%%tau%%%. %%%Tau%%% is a microtubule associated protein that is
aberrantly %%%phosphorylated%%% in %%%Alzheimer%%%'s disease of the
brain. Since c-fms expression is normally exclusive to cells of monocyte
lineage, these cells were examined for expression of %%%tau%%%. Heat
stable %%%tau%%% was identified in cultured peripheral blood monocytes.
This represents the first molecular characterization of %%%tau%%% in
cells of non-neural origin.

8/7/82 (Item 82 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07710219 BIOSIS NO.: 000092046000
ALTERED %%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEIN IN HEAT-SHOCKED RATS AND
PATIENTS WITH %%%ALZHEIMER%%% DISEASE
AUTHOR: PAPASOZOMENOS S C; SU Y
AUTHOR ADDRESS: DEP. PATHOL. LAB. MED., UNIV. TEXAS MED. SCH., HOUSTON,
TEX. 77030.
JOURNAL: PROC NATL ACAD SCI U S A 88 (10). 1991. 4543-4547. %%%1991%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the
United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Six hours after heat shocking 2- to 3-month-old male and female
Sprague-Dawley rats at 42.degree. C for 15 min, we analyzed .%%%tau%%%.
protein immunoreactivity in SDS extracts of cerebrums and peripheral
nerves by using immunoblot analysis and immunohistochemistry with the
anti-.%%%tau%%%. monoclonal antibody %%%Tau%%%-1, which recognizes a
phosphate-dependent non-%%%phosphorylated%%% epitope, and with
125I-labeled protein A. In the cerebral extracts, we found altered
%%%phosphorylation%%% of .%%%tau%%%. in heat-shocked females,
characterized by a marked reduction in the amount of nonphosphorylated .
%%%tau%%%., a doubling of the ratio of total (%%%phosphorylated%%% plus
nonphosphorylated) .%%%tau%%%. to nonphosphorylated .%%%tau%%%., and the
appearance of the slowest moving %%%phosphorylated%%% .%%%tau%%%.
polypeptide (68 kDa). Similar, but milder, changes were observed in male
rats. These changes progressively increased in females from 3 to 6 h
after heat shocking. In contrast, both %%%phosphorylated%%% .%%%tau%%%.
and nonphosphorylated .%%%tau%%%. were reduced in peripheral nerves after
heat shocking. In immunoblots of SDS extracts from %%%Alzheimer%%%
disease-affected brain, the two slowest moving %%%phosphorylated%%% .
%%%tau%%%. polypeptides (62 kDa and 66 kDa, respectively) were detected
by %%%Tau%%%-1 after dephosphorylation and by %%%Tau%%%-2 (an anti-.
%%%tau%%%. monoclonal antibody that recognizes a phosphate-independent
epitope) without prior dephosphorylation only in regions that contained .
%%%tau%%%. immunoreactivity in histologic preparations. In addition,
quantitative immunoblot analysis of cortex and the underlying white
matter with %%%Tau%%%-1 and 125I-labeled protein A showed that the amount
of %%%phosphorylated%%% .%%%tau%%%. progressively increased in the
%%%Alzheimer%%% disease-affected cerebral cortex, while concurrently a
proportionally lesser amount of .%%%tau%%%. entered the white matter
axons. The similar findings for the rat heat-shock model and
%%%Alzheimer%%% disease suggest that life stressors may play a role in
the etiopathogenesis of %%%Alzheimer%%% disease.

8/7/83 (Item 83 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07707758 BIOSIS NO.: 000092043539

CONTRASTING PATTERNS OF PROTEIN %%%PHOSPHORYLATION%%% IN HUMAN NORMAL AND
%%%ALZHEIMER%%% BRAIN FOCUS ON PROTEIN KINASE C AND PROTEIN F1-GAP-43
AUTHOR: FLOREZ J C; NELSON R B; ROUTTENBERG A
AUTHOR ADDRESS: DEP. NEUROBIOLOGY PHYSIOLOGY, NORTHWESTERN UNIV. EVANSTON,
IL 60208.
JOURNAL: EXP NEUROL 112 (3). 1991. 264-272. %%%1991%%%
FULL JOURNAL NAME: Experimental Neurology
CODEN: EXNEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We introduce a new procedure to study kinase substrates in postmortem human brain. By adding purified exogenous protein kinase C (PKC) and the phospholipid phosphatidylserine to brain homogenates in vitro we are able to analyze PKC substrates. A human 53-kDa phosphoprotein is described that appears to be homologous to rat and monkey protein F1 (GAP-43). This identity is based on molecular weight, isoelectric point, %%%phosphorylation%%% by exogenous protein kianse C, enhancement of its %%%phosphorylation%%% by three activators (phospholipids, calcium and phorbol esters), phosphopeptide maps, and cross-reactivity with an antibody raised against rat protein F1. Protein F1 is a PKC substrate associated with synaptic plasticity and nerve growth. Its %%%phosphorylation%%% in rat brain has been correlated with
long-term potentiation, an electrophysiological model of memory. In the present study of normal brain, human protein F1 shows an occipitotemporal in vitro %%%phosphorylation%%% gradient. This is consistent with previous observations in nonhuman primates. This gradient is less pronounced in %%%Alzheimer%%%'s disease (AD). Changes in the in vitro phsphorylation pattern of three other non-PKC substrates in %%%Alzheimer%%%'s disease,
including one with characteristics similar to microtubule-associated protein %%%tau%%%, are also reported. These results suggest that protein
%%%phosphorylation%%% can be studied in postmortem human brain and that
PKC-mediated %%%phosphorylation%%% of protein F1, already linked to synaptic plasticity and memory, may be altered in AD.

8/7/84 (Item 84 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07684754 BIOSIS NO.: 000092031675
METHODS IN LABORATORY INVESTIGATION HYDRATED AUTOCLAVE PRETREATMENT
ENHANCES %%%TAU%%% IMMUNOREACTIVITY IN FORMALIN-FIXED NORMAL AND
%%%ALZHEIMER%%%'S DISEASE BRAIN TISSUES
AUTHOR: SHIN R-W; IWAKI T; KITAMOTO T; TATEISHI J
AUTHOR ADDRESS: DEP. NEUROPATHOL., NEUROL. INST., FAC. MED., KYUSHU UNIV.
60, MAIDASHI, HIGASHI-KU, FUKUOKA 812, JPN.
JOURNAL: LAB INVEST 64 (5). 1991. 693-702. %%%1991%%%
FULL JOURNAL NAME: Laboratory Investigation
CODEN: LAINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We developed a new immunohistochemical method by which normal
%%%tau%%% antigenicity can be visualized in paraffin sections of formalin-fixed brain tissue. This method consists of autoclave pretreatment of sections immersed into distilled water (hydrated autoclaving) before incubation with anti-%%%tau%%% antibodies. In normal
human brain, immunoreactive %%%tau%%% was detected in neuronal cell bodies and dendrites, axon fibers, astroglia, oligodendroglia and gray matter neuropil. In previous studies on normal %%%tau%%% distribution, different optimized fixations that effectively preserve %%%tau%%% antigenicity were used but none of these revealed all of these compartments together. Our method is therefore considered to be more sensitive for detecting normal %%%tau%%% immunoreactivity. In addition, hydrated autoclaving had an enhancing effect on the abnormally %%%phosphorylated%%% (modified) %%%tau%%% immunoreactivity in formalin-fixed brains. In hydrated autoclaving of sections from patients with %%%Alzheimer%%%'s disease, neuropil threads, senile plaques, extracellular and intracellular tangles were enhanced in quantity and in staining intensity. Therefore, modified %%%tau%%% appears to accumulate
more densely than expected from conventional immunohistochemistry. Immunoblot analysis showed that normal or modified %%%tau%%% immunoreactivity was totally or partially eliminated on formalin treatment and could be revisualized by hydrated autoclaving, an event presumably related to recovering of formalin-masked %%%tau%%% antigens
through denaturation by hydrated autoclaving.

8/7/85 (Item 85 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07615129 BIOSIS NO.: 000091133013
%%%TAU%%% IN %%%ALZHEIMER%%%'S DISEASE AND DOWN'S SYNDROME IS INSOLUBLE AND
ABNORMALLY %%%PHOSPHORYLATED%%%
AUTHOR: HANGER D P; BRION J-P; GALLO J-M; CAIRNS N J; LUTHERT P J; ANDERTON
B H
AUTHOR ADDRESS: DEP. NEUROSCIENCE, INSTITUTE PSYCHIATRY, DE CRESPIGNY PARK,
DENMARK HILL, LONDON SE5 8AF, U.K.
JOURNAL: BIOCHEM J 275 (1). 1991. 99-104. %%%1991%%%
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Some investigators have described the presence in %%%Alzheimer%%%
's disease brain extracts of several abnormal forms of the microtubule-associated protein %%%tau%%%, based on their unusual mobility
in SDS-PAGE. It has been proposed that these abnormal forms of %%%tau%%%
may be the result of aberrant %%%tau%%% %%%phosphorylation%%%. In this
study we show that %%%tau%%% in extracts of %%%Alzheimer%%%'s disease
brain can be separated into two fractions based upon its solubility (100,000 g .times. 1 h supernatant) in non-denaturing conditions (100 mM-Mes, pH 6.5, 0.5 mM-MgCl2, 1 mM-EGTA and 1 M-NaCl). The %%%tau%%%
isoforms with decreased mobility in SDS/PAGE are predominantly in an insoluble fraction, whereas the soluble %%%tau%%% is indistinguishable by its mobility in SDS/PAGE from %%%tau%%% in soluble extracts of control brain. Insoluble %%%tau%%% displaying abnormal mobility on SDS/PAGE was
only found in %%%Alzheimer%%% and adult Down's syndrome brains and was
absent from the brains of age-matched controls and from fetal and infant Down's syndrome brains. There was a good correlation between the presence
of insoluble %%%tau%%% in brain extracts and the abundance of neurofibrillary tangles and senile neuritic plaques. The monoclonal antibody %%%Tau%%%.1 stained insoluble %%%tau%%% on Western blots only
after treatment of the nitrocellulose transfers with alkaline phosphatase, implying that this insoluble %%%tau%%% is in a particular state of %%%phosphorylation%%%. We conclude that, in %%%Alzheimer%%%'s
disease, a fraction of %%%tau%%% has a modified %%%phosphorylation%%%
state and a decreased solubility; these modifications may precede formation of the neurofibrillary tangles characteristic of %%%Alzheimer%%%'s disease and Down's syndrome in adults.

8/7/86 (Item 86 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07540137 BIOSIS NO.: 000091092215
A68 A MAJOR SUBUNIT OF PAIRED HELICAL FILAMENTS AND DERIVATIZED FORMS OF
NORMAL %%%TAU%%%
AUTHOR: LEE V M-Y; BALIN B J; OTVOS L JR; TROJANOWSKI J Q
AUTHOR ADDRESS: DEP. PATHOL. LAB. MED., UNIV. PENN. SCH. MED., PHILADELPHIA, PA. 19104, USA.
JOURNAL: SCIENCE (WASHINGTON D C) 251 (4994). 1991. 675-678. %%%1991%%%
FULL JOURNAL NAME: SCIENCE (Washington D C)
CODEN: SCIEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Putative %%%Alzheimer%%% disease (AD)-specific proteins (A68)
were purified to homogeneity and shown to be major subunits of one form of paired helical filaments (PHFs). The amino acid sequence and immunological data indicate that the backbone of A68 is indistinguishable from that of the protein %%%tau%%% (.%%%tau%%%.), but A68 could be distinguished from normal human .%%%tau%%%. by the degree to which A68
was %%%phosphorylated%%% and by the specific residues in A68 that served
as phosphate acceptors. The larger apparent relative molecular mass (Mr) of A68, compared to normal human .%%%tau%%%., was attributed to abnormal
%%%phosphorylation%%% of A68 because enzymatic dephosphorylation of A68
reduced its Mr to close to that of normal .%%%tau%%%.. Moreover, the LysSerProVal motif in normal human .%%%tau%%%. appeared to be an abnormal
%%%phosphorylation%%% site in A68 because the Ser in this motif was a phosphate acceptor site in A68, but not in normal human .%%%tau%%%.. Thus, the major subunits of a class of PHFs are A68 proteins and the excessive or inappropriate %%%phosphorylation%%% of normal .%%%tau%%%.
may change itys apparent Mr thus transforming .%%%tau%%%. into A68.

8/7/87 (Item 87 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07532956 BIOSIS NO.: 000040078745
%%%PHOSPHORYLATED%%% %%%TAU%%% IN %%%ALZHEIMER%%%'S DISEASE PAIRED HELICAL
FILAMENTS
AUTHOR: BAUM L; MASLIAH E; UEDA K; LIMOTO D; SAITOH T
AUTHOR ADDRESS: SCH. MED., DEP. NEUROSCI., M-024, LA JOLLA, CALIF. 92093.
JOURNAL: 20TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, ST. LOUIS,
MISSOURI, USA, OCTOBER 28-NOVEMBER 2, 1990. SOC NEUROSCI ABSTR 16 (2).
1990. 944. %%%1990%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/88 (Item 88 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07532952 BIOSIS NO.: 000040078741
%%%TAU%%% %%%PHOSPHORYLATION%%% IN HEAT-SHOCKED FEMALE AND MALE RATS AND
CEREBRAL EXPLANTS
AUTHOR: PAPASOZOMENOS S C; SU Y
AUTHOR ADDRESS: DEP. PATHOL., UNIV. TEXAS MED. SCH., HOUSTON, TX 77225.
JOURNAL: 20TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, ST. LOUIS,
MISSOURI, USA, OCTOBER 28-NOVEMBER 2, 1990. SOC NEUROSCI ABSTR 16 (2).
1990. 943. %%%1990%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/89 (Item 89 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07526493 BIOSIS NO.: 000091089622
ABNORMAL %%%PHOSPHORYLATION%%% OF %%%TAU%%% UBIQUITINATION IN
NEUROFIBRILLARY PATHOLOGY OF %%%ALZHEIMER%%% DISEASE
AUTHOR: BANCHER C; GRUNDKE-IQBAL I; IQBAL K; FRIED V A; SMITH H T;
WISNIEWSKI H M
AUTHOR ADDRESS: INSTITUTE BASIC RESEARCH, 1050 FOREST HILL ROAD, STATEN
ISLAND, NY 10314, USA.
JOURNAL: BRAIN RES 539 (1). 1991. 11-18. %%%1991%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: On tissue sections of %%%Alzheimer%%% brain, 4 antibodies to
%%%tau%%% immunolabel not only neurofibrillary tangles, neuritic plaques and neuropil threads but also the tangle-free cytoplasm of a subset of hippocampal and cortical neurons we believe to be at a stage of alteration preceding the formation of paired helical filaments (PHF). Pretreatment of tissue sections with alkaline phosphatase leads to an increase in staining intensity and in number of immunoreactive lesions with antibodies directed to an amino terminal and to a mid-region of the %%%tau%%% molecule. The diffuse neuronal staining could not be observed with any of 7 monoclonal antibodies recognizing ubiquitin. We conclude (1) that abnormal %%%phosphorylation%%% of %%%tau%%% occurs prior to its
incorporation into PHF and leads to its accumulation in the nerve cell body and (2) that ubiquitin is seen associated only when a neurofibrillary tangle is already formed.

8/7/90 (Item 90 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07524263 BIOSIS NO.: 000091087392
HUMAN NEUROBLASTOMA CELLS TREATED WITH ALUMINUM EXPRESS AN EPITOPE
ASSOCIATED WITH %%%ALZHEIMER%%%'S DISEASE NEUROFIBRILLARY TANGLES
AUTHOR: GUY S P; JONES D; MANN D M A; ITZHAKI R F
AUTHOR ADDRESS: MOLECULAR NEUROBIOLOGY LABORATORY, DEP. OPTOMETRY VISION
SCIENCES, UMIST, MANCHESTER M60 1QD, U.K.
JOURNAL: NEUROSCI LETT 121 (1-2). 1991. 166-168. %%%1991%%%
FULL JOURNAL NAME: Neuroscience Letters
CODEN: NELED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A number of studies have implicated aluminum as a possible factor
in the pathogenesis of %%%Alzheimer%%%'s disease (AD). Following an examination of the uptake of aluminum by human neuroblastoma cells in culture, treated with a range of concentrations of aluminum complexed with ethylene-diaminetetra-acetic acid (EDTA), we have now carried out an immunocytochemical study. Using an antibody to %%%phosphorylated%%%

%%%tau%%% protein, which reacts specifically with AD neurofibrillary tangles (NFT), we have found that after treatment periods of 16 days to 8 weeks with aluminum-EDTA, the cells show positive staining with this antibody. No such reaction was detected in cells grown in medium alone, nor in aluminum-EDTA-treated cells subjected to the same immunocytochemical procedure but without added primary antibody. Cells grown in medium plus EDTA, which contains a low level of aluminum contamination, showed a slight reaction. Our system may provide a suitable model for studying the early changes which lead to NFT formation.

8/7/91 (Item 91 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07501903 BIOSIS NO.: 000091075772
%%%TAU%%% IN %%%ALZHEIMER%%% NEUROFIBRILLARY TANGLES AMINO AND
CARBOXYL-TERMINAL REGIONS ARE DIFFERENTIALLY ASSOCIATED WITH PAIRED
HELICAL FILAMENTS AND THE LOCATION OF A PUTATIVE ABNORMAL
%%%PHOSPHORYLATION%%% SITE
AUTHOR: BRION J-P; HANGER D P; BRUCE M T; COUCK A-M; FLAMENT-DURAND J;
ANDERTON B H
AUTHOR ADDRESS: LAB. ANATOMIE PATHOL., MICROSCOPIE ELECTRONIQUE, UNIV.
LIBRE BRUXELLES, 808 ROUTE LENNIK, 1070-BRUSSELS, BELGIUM.
JOURNAL: BIOCHEM J 273 (1). 1991. 127-134. %%%1991%%%
FULL JOURNAL NAME: Biochemical Journal
CODEN: BIJOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: To investigate the extent to which whole %%%tau%%% proteins,
structurally abnormal %%%tau%%% and fragments of %%%tau%%% are incorporated into neurofibrillary tangles in %%%Alzheimer%%%'s disease, an immunocytochemical mapping study using a panel of antibodies to several synthetic human %%%tau%%% peptides has been performed. Neurofibrillary tangles were immunolabelled in situ, and paired helical filaments (PHF), the principal structural component of tangles, were immunolabelled after isolation and Pronase treatment. N-Terminal and C-terminal domains of %%%tau%%% were found to be present in tangles in situ. SDS-treated PHF were found to contain most of the C-terminal half of %%%tau%%% and were also labelled by antibodies to ubiquitin. Only some
of these PHF were labelled by antisera to %%%tau%%% sequences towards the
N-terminus, and this enabled the identification of a region of %%%tau%%% in which proteolytic cleavage may occur. The ultrastructural appearance of the immunolabelling suggested that both the N- and C-terminal domains of %%%tau%%% extend outwards from the axis of PHF. After Pronase treatment, PHF were strongly labelled only by an antiserum to PHF and by the antiserum to the most C-terminal %%%tau%%% synthetic peptide. The latter antiserum also strongly labelled extracellular tangles in situ, whereas these extracellular tangles were poorly labelled by the antisera to the other synthetic peptides. One anti-(%%%tau%%% peptide) serum labelled a population of neurofibrillary tangles in situ only after alkaline phosphatase pretreatment of tissue sections. Our results show that, although peptides along the length of the %%%tau%%% molecule are associated with neurofibrillary tangles in situ, only the C-terminal one-third of the molecule is tightly associated with PHF, since this region of %%%tau%%% is resistant to SDS treatment of PHF. We also report
the existence in PHF in situ of a masked %%%tau%%% epitope which is partially unmasked by dephosphorylation. These results are indicative of post-translational changes in tangle-associated %%%tau%%% in degenerating
neurons in %%%Alzheimer%%%'s disease.

8/7/92 (Item 92 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07424047 BIOSIS NO.: 000091030036
%%%PHOSPHORYLATION%%% CHARACTERISTICS OF THE A68 PROTEIN IN %%%ALZHEIMER%%%
'S DISEASE
AUTHOR: VINCENT I J; DAVIES P
AUTHOR ADDRESS: ALBERT EINSTEIN COLL. MED., DEP. PATHOL., F526, 1300 MORRIS
PARK AVENUE, BRONX, NY 10461, USA.
JOURNAL: BRAIN RES 531 (1-2). 1990. 127-135. %%%1990%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: As a first step in understanding the function of the 68-kDa Alz-50 antigen (A68) in the pathophysiology of %%%Alzheimer%%%'s disease
(AD), we have reexamined preliminary observations in our laboratory (Wolozin and Davies, 1986) of a protein kinase activity associated with crude preparations of the protein. This study was undertaken to determine whether the kinase activity is an inherent property of the Alz-50 antigen, or is a property of an associated protein.
%%%Phosphorylation%%%
was therefore examined by incubating A68-enriched preparations with radiolabelled ATP. This resulted in the appearance of a labelled 68-kDa phosphoprotein, comigrating with the Alz-50 reactive A68 protein. The labelling of this 68-kDa protein occurred in the presence of 2% SDS, suggesting that it is more likely to represent an autophosphorylation than a transfer of phosphate mediated by another kinase. Upon further inspection, it was found that the autophosphorylated 68-kDa protein was not localized to regions of AD brain where A68 was detectable, but displayed a more ubiquitous distribution. In addition, this phosphoprotein was also observed to be present in similar preparations from normal brain, which lacked the Alz-50 antigen (Wolozin et al, 1986). These findings indicate that the auto-kinase activity at 68 kDa is not closely associated with the A68 protein, but with a comigrating contaminant in the preparation. Other experiments in this study indicate that A68 is not a substrate for in vitro phophorylation. Following incubation of A68 preparations with radiolabelled ATP, immunoprecipitation of the antigen did not reveal any phosphate transfer to the protein. These results were unaffected by a prior incubation with alkaline phosphatase, even when the subsequent %%%phosphorylation%%% reactions were conducted in the presence of protein kinase activators. Incubation with alkaline phosphatase did not produce any alterations in electrophoretic mobility of A68, nor did it affect the binding of antibodies directed against phosphatase-sensitive epitopes with A68. Thus, despite the suggestion that A68 is a modified form of %%%tau%%%, the antigen exhibits remarkable differences from %%%tau%%% with regard to
its sensitivity to kinases and to alkaline phosphatase.

8/7/93 (Item 93 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07416402 BIOSIS NO.: 000040030711
%%%PHOSPHORYLATION%%% OF MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% BY CAM
KINASE AND OTHER PROTEIN KINASES
AUTHOR: STEINERT B; MANDELKOW E-M; BIERNAT J; GUSTKE N; MEYER H E; SCHMIDT
B; MIESKES G; SOELING H D; DRECHSEL D; ET AL
AUTHOR ADDRESS: MAX-PLANCK-UNIT STRUCTURAL MOLECULAR BIOL., HAMBURG, W.
GER.
JOURNAL: THIRTIETH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY,
SAN DIEGO, CALIFORNIA, USA, DECEMBER 9-13, 1990. J CELL BIOL 111 (5 PART
2). 1990. 437A. %%%1990%%%
CODEN: JCLBA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation

LANGUAGE: ENGLISH

8/7/94 (Item 94 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07416391 BIOSIS NO.: 000040030700
THE SELECTIVE %%%PHOSPHORYLATION%%% OF SITES NEAR THE MICROTUBULE MT
BINDING DOMAIN IN NORMAL %%%TAU%%% MAY BE AN INITIAL EVENT LEADING TO THE
FORMATION OF %%%ALZHEIMER%%% DISEASE AD PAIRED HELICAL FILAMENTS PHF
AUTHOR: ROSENBLUM J S; BRAMBLETT G T; LEE V M-Y
AUTHOR ADDRESS: DEP. PATHOL. AND LAB. MED., UNIV. PA. SCH. MED., PHILADELPHIA, PA. 19104.
JOURNAL: THIRTIETH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY,
SAN DIEGO, CALIFORNIA, USA, DECEMBER 9-13, 1990. J CELL BIOL 111 (5 PART
2). 1990. 435A. %%%1990%%%
CODEN: JCLBA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/95 (Item 95 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07410664 BIOSIS NO.: 000040024973
CYTOSKELETAL PROTEIN PATHOLOGY IN %%%ALZHEIMER%%%'S DISEASE PROTEIN
%%%PHOSPHORYLATION%%% AND UBIQUITINATION
AUTHOR: IQBAL K; GRUNDKE-IQBAL I
AUTHOR ADDRESS: N.Y. STATE INST. BASIC RES. DEV. DISABILITIES, 1050 FOREST
HILL ROAD, STATEN ISLAND, N.Y. 10314, USA.
JOURNAL: MIYATAKE, T., D. J. SELKOE AND Y. IHARA (ED.). INTERNATIONAL
CONGRESS SERIES, 884. MOLECULAR BIOLOGY AND GENETICS OF ALZHEIMER'S
DISEASE; INTERNATIONAL SYMPOSIUM ON DEMENTIA, NIIGATA, JAPAN, NOVEMBER
11-14, 1989. XV+288P. ELSEVIER SCIENCE PUBLISHERS B.V. (BIOMEDICAL
DIVISION): AMSTERDAM, NETHERLANDS; (DIST. FOR THE USA AND CANADA BY
ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK). ILLUS. ISBN
0-444-81112-5. 0 (0). 1990. 47-56. %%%1990%%%
CODEN: EXMDA
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/96 (Item 96 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07410661 BIOSIS NO.: 000040024970
THE %%%PHOSPHORYLATION%%% SITE OF THE %%%TAU%%% IN PAIRED HELICAL FILAMENTS
AN IMMUNOCHEMICAL APPROACH
AUTHOR: IHARA Y; MIURA R; KONDO J; HAYASE T
AUTHOR ADDRESS: 2ND LAB. CLIN. PHYSIOL., TOKYO METROPOLITAN INST.
GERONTOL., ITABASHI-KU, TOKYO 173, JAPAN.
JOURNAL: MIYATAKE, T., D. J. SELKOE AND Y. IHARA (ED.). INTERNATIONAL
CONGRESS SERIES, 884. MOLECULAR BIOLOGY AND GENETICS OF ALZHEIMER'S
DISEASE; INTERNATIONAL SYMPOSIUM ON DEMENTIA, NIIGATA, JAPAN, NOVEMBER
11-14, 1989. XV+288P. ELSEVIER SCIENCE PUBLISHERS B.V. (BIOMEDICAL
DIVISION): AMSTERDAM, NETHERLANDS; (DIST. FOR THE USA AND CANADA BY
ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK). ILLUS. ISBN
0-444-81112-5. 0 (0). 1990. 21-28. %%%1990%%%
CODEN: EXMDA
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/97 (Item 97 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07376558 BIOSIS NO.: 000091003238
THE HUMAN PINEAL GLAND IN AGING AND %%%ALZHEIMER%%%'S DISEASE PATTERNS OF
CYTOSKELETAL ANTIGEN IMMUNOREACTIVITY
AUTHOR: PARDO C A; MARTIN L J; TRONCOSO J C; PRICE D J
AUTHOR ADDRESS: DEP. PATHOL., JOHNS HOPKINS UNIV. SCH. MED., 600 NORHT
WOLFE ST., BALTIMORE, MD. 21205-2181, USA.
JOURNAL: ACTA NEUROPATHOL 80 (5). 1990. 535-540. %%%1990%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Patients with %%%Alzheimer%%%'s disease (AD) and some aged
controls may have diminished functions of the pienal gland. In this immunocytochemical study, we stained pineal glands from cases of AD and young and aged cotnrols for cytoskeletal elements and amyloid. We found no evidence of neurofibrillary tangles (NFT) or the accumulation of neurofilaments, %%%tau%%%, A68, or .beta./A4 amyloid deposition in pinealocytes or associated structures in cases of AD or controls. In both AD and controls, we observed dense immunoreactivity for %%%phosphorylated%%% neurofilaments in marginal plexuses associated with
processes of pinealocytes, boutons, and knob-like endings. The accumulation of %%%phosphorylated%%% neurofilaments in the processes of
pinealocytes appears to be a normal morphological characteristic of the pineal gland and may not represent a pathological change.

8/7/98 (Item 98 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07375324 BIOSIS NO.: 000091002004
%%%PHOSPHORYLATION%%% OF MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%%
IDENTIFICATION OF THE SITE FOR CALCIUM CALMODULIN DEPENDENT KINASE AND
RELATIONSHIP WITH %%%TAU%%% %%%PHOSPHORYLATION%%% IN %%%ALZHEIMER%%%
TANGLES
AUTHOR: STEINER B; MANDELKOW E-M; BIERNAT J; GUSTKE N; MEYER H E; SCHMIDT B
; MIESKES G; SOELING H D; DRECHSEL D; ET AL
AUTHOR ADDRESS: INQ. E. MANDEKOW, MAX-PLANCK-UNIT STRUCTURAL MOL. BIOL.,
C/O DESY, NOTKESTRASSE 85, D-2000 HAMBURG 52, W. GER.
JOURNAL: EMBO (EUR MOL BIOL ORGAN) J 9 (11). 1990. 3539-3544. %%%1990%%%
FULL JOURNAL NAME: EMBO (European Molecular Biology Organization) Journal
CODEN: EMJOD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The microtubule array in neuronal cells undergoes extensive growth, dynamics and rearrangements during neurite outgrowth. While

little is known about how these changes are regulated,
microtuble-associated proteins (MAPs) including %%%tau%%% protein are likely to perform an important role. %%%Tau%%% is one of the MAPs in mammalian brain. When isolated it is usually a mixture of several isoforms containing between 341 and 441 residues that arise from alternative splicing. %%%Tau%%% can be %%%phosphorylated%%% by several
protein kinases. %%%Phosphorylation%%% at certain sites results in major structural and functional changes, as seen by changes in electrophoretic mobility, interaction with microtubules, molecular length and elasticity. Here we show that the sites of %%%phosphorylation%%% by four kinases (PKA, PKC, CK and CaMK) all lie in the C-terminal microtubule-binding half of %%%tau%%%, but only the %%%phosphorylation%%% by CaM kinase shows
the pronounced shift in electrophoretic mobility characteristic for %%%tau%%% from %%%Alzheimer%%% neurofibrillary tangels. By using a combination of limited proteolysis, protein sequencing and protein engineering we show that a single %%%phosphorylation%%% site is responsible for this shift, located at Ser 405 in the C-terminal tail of the protein outside the region of internal repeats.
%%%Phosphorylation%%%
at this site not only reduces the electrophoretic mobility of %%%tau%%%, it also makes the protein long and stiff, as shown earlier. The site is likely to be %%%phosphorylated%%% in %%%tau%%% from %%%Alzheimer%%%
neurofibrillary tangles.

8/7/99 (Item 99 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07358870 BIOSIS NO.: 000090137781
ALZ-50 RECOGNIZES A %%%PHOSPHORYLATED%%% EPITOPE OF %%%TAU%%% PROTEIN
AUTHOR: UEDA K; MASLIAH E; SAITOH T; BAKALIS S L; SCOBLE H; KOSIK K S
AUTHOR ADDRESS: DEP. NEUROSCIENCES, SCHOOL MEDICINE, UNIVERSITY CALIFORNIA
AT SAN DIEGO, LA JOLLA, CALIF. 92093.
JOURNAL: J NEUROSCI 10 (10). 1990. 3295-3304. %%%1990%%%
FULL JOURNAL NAME: Journal of Neuroscience
CODEN: JNRSD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alz-50 is a monoclonal antibody that detects antigens enriched in
the brain tissue of %%%Alzheimer%%%'s disease (AD) patients. Although Alz-50 recognizes .%%%tau%%%., an identified integral constituent of the AD paired helical filament (PHF), the exact nature of the antigenic site is unknown. An immunoblot analysis demonstrated that the antigenic sites to Alz-50 are diminished by acid phosphatase treatment. Consistent with this finding, Alz-50 antigens were more concentrated in brain homogenates prepared with phosphatase inhibitors. The epitope in .%%%tau%%%. with which Alz-50 reacts is located in the carboxy terminus within a 14-amino acid region from just beyond the microtubule-binding repeats to the carboxy terminus. An isolated carboxy-terminal chymotryptic peptide from bovine brain .%%%tau%%%.-reactive with Alz-50 was analyzed by fast-atom-bombardment mass spectroscopy (FAB-MS) and was found to be present as both a monophosphopeptide and a nonphosphorylated peptide. The
immunohistological analysis has demonstrated that Alz-50 staining of neurofibrillary tangles (NFTs) is sensitive to acid phosphatase but not to alkaline phosphatase. Furthermore, Alz-50 staining of NFTs was effectively adsorbed by a high concentration of phosphoserine but not by serine or phosphothreonine. These results strongly suggest that Alz-50 recognizes a %%%phosphorylated%%% epitope in the carboxy terminus of . %%%tau%%%. which has not been previously detected by using alkaline phosphatase. The strong Alz-50 staining in AD samples may represent another association between a %%%phosphorylation%%% state and neurofibrillary lesions. As a marker of the inchoate tangle-bearing neuron, the characterization of the Alz-50 epitope in .%%%tau%%%. offers
a partial molecular basis for the modifications that contribute to the assembly of PHFs.

8/7/100 (Item 100 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07298218 BIOSIS NO.: 000090078105
CORRELATION BETWEEN MICROSCOPICAL CHANGES AND %%%TAU%%% 64 AND 69
BIOCHEMICAL DETECTION IN SENILE DEMENTIA OF THE %%%ALZHEIMER%%% TYPE
%%%TAU%%% 64 AND 69 ARE RELIABLE MARKERS OF THE NEUROFIBRILLARY
DEGENERATION
AUTHOR: FLAMENT S; DELACOURTE A; DELAERE P; DUYCKAERTS C; HAUW J-J
AUTHOR ADDRESS: LAB. DE NEUROSCI., U16 INSERM, FACULTE DE MEDECINE, F-59045
LILLE, FRANCE.
JOURNAL: ACTA NEUROPATHOL 80 (2). 1990. 212-215. %%%1990%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have recently reported that the immunoblot detection of two
abnormally %%%phosphorylated%%% %%%tau%%% proteins, named %%%Tau%%% 64
and 69, in homogenates of cortical areas from patients with %%%Alzheimer%%%'s disease (AD) was systematically associated with the presence of neurofibrillary tangles (NFT) and senile plaques (SP) in these areas. A blind study was performed to confirm that these proteins had a reliable diagnostic value and to study more precisely the correlation between %%%Tau%%% 64 and 69 and the presence of the characteristic lesions of AD. The density of NFT and of SP was evaluated on histological sections of gyrus supramarginalis from 17 patients with graded intellectual status. Immunodetection of %%%Tau%%% 64 and 69 was
semiquantitatively evaluated by densitometry (reflectance mode) on immunoblots of homogenates of the same area on the contralateral hemisphere. The statistical analysis of results showed that %%%Tau%%% 64
and 69 were more strongly correlated with NFT than with SP. Moreover, semiquantitative evaluation of %%%Tau%%% 64 and 69 was correlated with
the intellectual status (BTS score). Therefore, these pathological forms of %%%tau%%% proteins are reliable markers of the presence of NFT and SP
in the neocortex and may be used as a diagnostic tool.

8/7/101 (Item 101 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07298210 BIOSIS NO.: 000090078097
PATHOLOGICAL PROTEINS %%%TAU%%% 64 AND 69 ARE SPECIFICALLY EXPRESSED IN THE
SOMATODENDRITIC DOMAIN OF THE DEGENERATING CORTICAL NEURONS DURING
%%%ALZHEIMER%%%'S DISEASE DEMONSTRATION WITH A PANEL OF ANTIBODIES
AGAINST %%%TAU%%% PROTEINS
AUTHOR: DELACOURTE A; FLAMENT S; DIBE E M; HUBLAU P; SABLONNIERE B; HEMON B
; SHERRER V; DEFOSSEZ A
AUTHOR ADDRESS: A.D.E.R.M.A., UNITE INSERM 156, FAC. MED. LILLE, F-59045
LILLE CEDEX, FR.
JOURNAL: ACTA NEUROPATHOL 80 (2). 1990. 111-117. %%%1990%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Bundles of paired helical filaments (PHF) accumulate in the

pyramidal neurons that degenerate during %%%Alzheimer%%%'s disease. This
neurofibrillary degeneration is highly correlated with clinical signs of dementia. During this degeneration process, %%%Tau%%% proteins, which are
the major antigenic components of PHF, are abnormally %%%phosphorylated%%% and two pathological isoforms named %%%Tau%%% 64 and
69 are expressed. We have studied their immunoblot distribution in the cortical gray and white matter from different reginons of normal and %%%Alzheimer%%% brains, to determine if the degenerating process preferentially affects the somatodendritic or the axonal domain. Two categories of antibodies were used. The first category consisted of anti-human native %%%Tau%%%, anti-%%%Tau%%% proteins from different
vertebrates, anti-PHF, monoclonal antibody Alz-50 and an anti-C terminal repeated region of %%%Tau%%%. In control brains, these antibodies strongly detected normal %%%Tau%%% proteins in the gray matter while %%%Tau%%% immunodetection was weak in the white matter. In %%%Alzheimer%%% brain cortices, each antibody detected %%%Tau%%% 64 and
69 in gray matter extracts but not at all in white matter extracts. The second category of anti-%%%Tau%%% consisted of the anti-PHF saturated with normal brain protein extracts. This antiserum only probed the abnormally %%%phosphorylated%%% %%%Tau%%% proteins. It detected %%%Tau%%%
64 and 69 exclusively in the cortical gray matter of %%%Alzheimer%%% brains. Moreover, a 55-kDa %%%Tau%%% protein was also immunolabelled, which might be an intermediary form between normal %%%Tau%%% and %%%Tau%%% 64 and 69. Our results demonstrate that %%%Tau%%% proteins are
normal and major components of the somatodendritic domain and that %%%Tau%%% pathology, reflected by the presence of %%%Tau%%% 64 and 69,
affects preferentially this domain during %%%Alzheimer%%%'s disease.

8/7/102 (Item 102 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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07273626 BIOSIS NO.: 000090053508
%%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEINS A MAJOR EVENT DURING THE
PROCESS OF NEUROFIBRILLARY DEGENERATION A COMPARATIVE STUDY BETWEEN
%%%ALZHEIMER%%%'S DISEASE AND DOWN'S SYNDROME
AUTHOR: FLAMENT S; DELACOURTE A; MANN D M A
AUTHOR ADDRESS: UNITE INSERM 16, LAB. DE NEUROSCI., FAC. DE MED., PLACE DE
VERDUN 59045 LILLE, FRANCE.
JOURNAL: BRAIN RES 516 (1). 1990. 15-19. %%%1990%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Six different brain areas from 6 patients with Down's syndrome
(DS) of different ages were studied in respect of their %%%Tau%%% protein
content using the western-blot technique. They were also studied histologically using a Palmgren (silver staining) method in order to reveal the presence of NFT and SP. The results of these studies show that %%%Tau%%% 64 and 69, two pathological %%%Tau%%% variants recently described in the brains of patients with %%%Alzheimer%%%'s disease (AD),
are also present in the brains of patients with DS. Alkaline phosphatase treatment demonstrates that their heavy molecular weight is due, as in AD, to an abnormal %%%phosphorylation%%% of %%%Tau%%% proteins. The
results of this study show that the detection of %%%Tau%%% 64 and 69 in
the brain of these patients is correlated with the presence of neurofibrillary tangles (NFT) and senile plaques (SP). These findings confirm that DS can act as a model for the study of the pathological events that occur in AD. Moreover, they suggest that the abnormal %%%phosphorylation%%% of %%%Tau%%% proteins, enhancing a shift of their
electrophoretic mobility, might be an important step among the sequence of events that characterize neurofibrillary degeneration.

8/7/103 (Item 103 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

07201174 BIOSIS NO.: 000039115528
%%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEIN
AUTHOR: UCHIDA T; ISHIGURO K
AUTHOR ADDRESS: MITSUBISI KASEI INST. OF LIFE SCI.
JOURNAL: JPN J GERIATR 27 (3). 1990. 280-286. %%%1990%%%
FULL JOURNAL NAME: Japanese Journal of Geriatrics
CODEN: NIRZA
RECORD TYPE: Citation
LANGUAGE: JAPANESE

8/7/104 (Item 104 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

07128283 BIOSIS NO.: 000039064977
PAIRED HELICAL FILAMENTS PHF IN %%%ALZHEIMER%%% DISEASE ARE
%%%PHOSPHORYLATED%%% AT MULTIPLE SITES
AUTHOR: MURTHY L R; IQBAL K
AUTHOR ADDRESS: INST. BASIC RES. DEV. DISABILITIES, STATEN ISLAND, N.Y.
10314, USA.
JOURNAL: SECOND INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, TORONTO, ONTARIO, CANADA, JULY 15-20, 1990. NEUROBIOL AGING 11
(3). 1990. 285. %%%1990%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/105 (Item 105 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

07128282 BIOSIS NO.: 000039064976
THE NEURONAL ANTIGEN A68 RECOGNIZED BY ALZ-50 IN AD BRAINS IS AN ABNORMALLY
%%%PHOSPHORYLATED%%% %%%TAU%%% PROTEIN
AUTHOR: FLAMENT S; BUEE L; DELACOURTE A
AUTHOR ADDRESS: LAB. INSERM NEUROSCIENCES, FAC. MED., LILLE 59045, FRANCE.
JOURNAL: SECOND INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, TORONTO, ONTARIO, CANADA, JULY 15-20, 1990. NEUROBIOL AGING 11
(3). 1990. 284-285. %%%1990%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/106 (Item 106 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

07128268 BIOSIS NO.: 000039064962
ABNORMALLY %%%PHOSPHORYLATED%%% %%%TAU%%% ISOLATED FROM %%%ALZHEIMER%%%
DISEASE BRAIN CYTOSOL IS NOT UBIQUITINATED
AUTHOR: KOEPKE-SECUNDO E; GRUNDKE-IQBAL I; IQBAL K

AUTHOR ADDRESS: INST. BASIC RES. DEV. DISABILITIES, 1050 FOREST HILL ROAD,
STATEN ISLAND, N.Y. 10314, USA.
JOURNAL: SECOND INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, TORONTO, ONTARIO, CANADA, JULY 15-20, 1990.
NEUROBIOL AGING 11
(3). 1990. 281. %%%1990%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/107 (Item 107 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07128267 BIOSIS NO.: 000039064961
ABNORMAL %%%PHOSPHORYLATION%%% OF %%%TAU%%% PRECEDES UBIQUITINATION IN
NEUROFIBRILLARY PATHOLOGY OF %%%ALZHEIMER%%% DISEASE
AUTHOR: BANCHER C; GRUNDKE-IQBAL I; IQBAL K; FRIED V A; SMITH H T;
WISNIEWSKI H M
AUTHOR ADDRESS: NYS INST. BASIC RES., STATEN ISLAND, N.Y.
JOURNAL: SECOND INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, TORONTO, ONTARIO, CANADA, JULY 15-20, 1990.
NEUROBIOL AGING 11
(3). 1990. 281. %%%1990%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/108 (Item 108 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07128264 BIOSIS NO.: 000039064958
STRUCTURE ELASTICITY AND %%%PHOSPHORYLATION%%% OF MICROTUBULE-ASSOCIATED
PROTEIN %%%TAU%%%
AUTHOR: MANDELKOW E M; LICHTENBERG B; HAGESTEDT T; WILLE H; MANDELKOW E
AUTHOR ADDRESS: MAX-PLANCK-UNIT FOR STRUCTURAL MOL. BIOL., C/O DESY,
NOTKESTRASSE 85, D-2000 HAMBURG 52, FRG.
JOURNAL: SECOND INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE AND RELATED
DISORDERS, TORONTO, ONTARIO, CANADA, JULY 15-20, 1990.
NEUROBIOL AGING 11
(3). 1990. 280. %%%1990%%%
CODEN: NEAGD
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/109 (Item 109 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07038474 BIOSIS NO.: 000089120029
%%%ALZHEIMER%%% DISEASE PROTEINS A68 SHARE EPITOPES WITH %%%TAU%%% BUT SHOW
DISTINCT BIOCHEMICAL PROPERTIES
AUTHOR: KSIEZAK-REDING H; BINDER L I; YEN S-H
AUTHOR ADDRESS: DEP. PATHOL., ALBERT EINSTEIN COLL. MED., 1300 MORRIS PARK
AVE., BRONX, N.Y. 10461.
JOURNAL: J NEUROSCI RES 25 (3). 1990. 420-430. %%%1990%%%
FULL JOURNAL NAME: Journal of Neuroscience Research
CODEN: JNRED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Alz 50, a monoclonal antibody raised against %%%Alzheimer%%% brain homogenate, reacts with neurofibrillary tangles, microtubule-associated proteins %%%tau%%%, and %%%Alzheimer%%% brain proteins of molecular weight 70-60 kDa (A68). To study the relationship between A68 and normal human %%%tau%%% we compared the biochemical properties of these proteins and tested the reactivity of A68 with eight antibodies (Alz 50, %%%Tau%%% 60, %%%Tau%%%-2, %%%Tau%%% 14, %%%Tau%%%-1, Ab 636.7, NP14, %%%Tau%%% 46) that bind to various regions of %%%tau%%% molecule. On Western blots, all %%%tau%%%-reactive antibodies, except %%%Tau%%%-1, recognized A68. Pretreatment with alkaline phosphatase was required for the %%%Tau%%%-1 binding to A68. A68 consisted of three polypeptides of 68, 64, and 60 kDa, while %%%tau%%% contained 4-6 polypeptides of 50-65 kDa. A68 was less heterogenous than %%%tau%%% in the number of pI variants on two-dimensional gels. All A68 variants were more acidic (pI 5.5-6.5) than human %%%tau%%% (pI 6.5-8.5). Phosphatase treatment had only a minor effect on the pI and mobility of A68. Limited proteolysis of A68 with trypsin or chymotrypsin generated large fragments of 56-66 kDa (chymotrypsin) and 40-45 kDa (trypsin). While none of the fragments was recognized by Alz 50, the chymotryptic fragments were reactive with all the other %%%tau%%% antibodies, and the tryptic fragments were positive with five of the antibodies (%%%Tau%%% 14, %%%Tau%%%-1, Ab 636.7, NP14, and %%%Tau%%% 46). The peptide maps of A68 differed from that of %%%tau%%% in the number and the size of the peptide fragments. The differences in biochemical properties of these proteins and the sharing multiple epitopes suggest that A68 is a modified form of %%%tau%%%. The modification in part may be due to %%%phosphorylation%%%, although other changes rendering different isoelectrical properties and susceptibility to proteases need to be considered. The removal of the Alz 50 epitope by a cleavage of a 2-3 kDa fragment which does not contain the most C-terminal epitope (%%%Tau%%% 46) indicates that the Alz 50 epitope is located at the N-terminal periphery of the A68 molecule.

8/7/110 (Item 110 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06994610 BIOSIS NO.: 000089095874
ABERRANT CASEIN KINASE II IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: IIMOTO D S; MASLIAH E; DE TERESA R; TERRY R D; SAITOH T
AUTHOR ADDRESS: DEP. NEUROSCI., SCH. MED., UNIV. CALIFORNIA SAN DIEGO, LA
JOLLA, CALIF. 92093, USA.
JOURNAL: BRAIN RES 507 (2). 1990. 273-280. %%%1990%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Abnormal protein %%%phosphorylation%%% has been identified in %%%Alzheimer%%%'s disease (AD) for several proteins including a Mr 60,000 protein, a Mr 86,000 protein and a microtubule-associated protein . %%%tau%%%.. The Mr 86,000 protein is %%%phosphorylated%%% by protein kinase C, whereas protein kinases responsible for other aberrant %%%phosphorylation%%% reactions are not known. In addition to protein kinase C, another kinase, casein kinase II (CK-II), has now been shown to be aberrant in AD. The spermine-dependent CK-II activity is reduced by

84% in AD and the amount of CK-II as determined by its immunoreactivity on a Western blot is reduced by 63%. Furthermore, the distribution of CK-II in AD is altered. Although the neuronal cell body reacts well with CK-II antisera in the normal cortex, the non-tangle-bearing neurons in the AD cortex showed a 15-30% decrease in anti-CK-II immunoreactivity. The neurofibrillary tangles, on the other hand, stain very strongly with rabbit anti-CK-II and indicates that CK-II may be involved in the pathology of AD. The study of CK-II immunoreactivity for dementing diseases other than AD revealed a similar reduction, suggesting the CK-II involvement in the common process of neurodegeneration.

8/7/111 (Item 111 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06951732 BIOSIS NO.: 000089073737
HIPPOCAMPAL NEURONS PREDISPOSED TO NEUROFIBRILLARY TANGLE FORMATION ARE
ENRICHED IN TYPE II CALCIUM CALMODULIN-DEPENDENT PROTEIN KINASE
AUTHOR: MCKEE A C; KOSIK K S; KENNEDY M B; KOWALL N W
AUTHOR ADDRESS: DEP. NEUROPATHOL., MASS. GEN. HOSP., BOSTON, MASS. 02114.
JOURNAL: J NEUROPATHOL EXP NEUROL 49 (1). 1990. 49-63.
%%%1990%%%
FULL JOURNAL NAME: Journal of Neuropathology & Experimental Neurology
CODEN: JNENA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The microtubule-associated phosphoprotein, %%%tau%%%, is an
integral component of paired helical filaments in %%%Alzheimer%%% neurofibrillary tangles (NFT). The mechanism of NFT formation is unknown but aberrant %%%phosphorylation%%% of %%%tau%%% may be contributory.
Calcium/calmodulin-dependent protein kinase type II (CaM kinase II), the most abundant kinase in the brain, %%%phosphorylates%%% %%%tau%%% in
vitro. We found CaM kinase II immunoreactivity concentrated in human hippocampal pyramidal neurons of CA1 and the subiculum. In %%%Alzheimer%%%'s disease (AD) staining intensity of CA1 and subicular neurons is strikingly increased despite NFT formation and neuronal depletion. Enhanced CaM kinase II activity, possibly a result of deafferentation, may contribute to %%%phosphorylation%%% of %%%tau%%%
protein leading to NFT deposition and neuronal death in AD.

8/7/112 (Item 112 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06951730 BIOSIS NO.: 000089073735
MODIFIED BIELSCHOWSKY AND IMMUNOCYTOCHEMICAL STUDIES ON CEREBELLAR PLAQUES
IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: SUENAGA T; HIRANO A; LLENA J F; KSIEZAK-REDING H; YEN S-H; DICKSON
D W
AUTHOR ADDRESS: DIV. NEUROPATHOL., DEP. PATHOL., MONTEFIORE MED. CENT., 111
E. 210TH ST., BRONX, N.Y. 10467.
JOURNAL: J NEUROPATHOL EXP NEUROL 49 (1). 1990. 31-40.
%%%1990%%%
FULL JOURNAL NAME: Journal of Neuropathology & Experimental Neurology
CODEN: JNENA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Senile plaques (SP) in the cerebellum of 23 cases of %%%Alzheimer%%%'s disease (AD), three with widespread amyloid angiopathy,
were studied with a modified Bielschowsky stain and immunocytochemical methods using antibodies to a beta-amyloid synthetic peptide (.beta.ASP), %%%phosphorylated%%% neurofilament proteins, ubiquitin, %%%tau%%% protein, and glial fibrillary acidic protein (GFAP). The four subtypes of SP (diffuse plaques, compact plaques, perivascular plaques, and subpial fibrillar deposits) that were observed with the modified Bielschowsky stain were also stained with antibodies to .beta.ASP. Many cerebellar SP contained ubiquitin-positive granular elements resembling dystrophic neurites. In contrast to neuritic elements in cerebral SP in AD, ubiquitin-positive elements in cerebellar Sp were not labeled with antibodies to %%%phosphorylated%%% neurofilament or %%%tau%%% proteins.
Various degrees of glial reaction were observed in all subtypes of SP except diffuse plaques. The absence of %%%phosphorylated%%% neurofilament
and %%%tau%%% epitopes in neuritic elements in cerebellar SP is not surprising since paired helical filaments have not been seen in the cerebellum. Nevethereless, our results suggest that cerebellar SP are frequently associated with dystrophic neurites.

8/7/113 (Item 113 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06867202 BIOSIS NO.: 000089016793
ABNORMAL PROCESSING OF MULTIPLE PROTEINS IN %%%ALZHEIMER%%% DISEASE
AUTHOR: ZHANG H; STERNBERGER N H; RUBINSTEIN L J; HERMAN M M; BINDER L I;
STERNBERGER L A
AUTHOR ADDRESS: DEP. NEUROL., UNIV. MARYLAND SCH. MED., BALTIMORE, MD.
21201.
JOURNAL: PROC NATL ACAD SCI U S A 86 (20). 1989. 8045-8049.
%%%1989%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the
United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Cerebrovascular amyloid is the main constituent of the perivascular and neuritic plaques typical of %%%Alzheimer%%% disease, whereas neurofilaments and microtubule-associated %%%tau%%% protein have
been considered primary contributors to the formation of the characteristic %%%Alzheimer%%% tangles. Plaques and tangles and their constituents have at times been ascribed a role in pathogenesis of the disease. Normally, neurofilaments become %%%phosphorylated%%% only upon
axonal entry. In many neurologic disorders, neurofilament %%%phosphorylation%%%, as detected by any of the available monoclonal antibodies (mAbs) to neurofilament %%%phosphorylated%%% epitopes is shifted from an axonal to a cell-body location. An exception is provided by %%%Alzheimer%%% disease, where tangles (which are neuronal cell-body-derived structures) exhibit only one %%%phosphorylated%%% epitope. However, the very presence of neurofilaments in tangles and plaques has been questioned because of a reported cross-reaction of mAbs to %%%phosphorylated%%% neurofilaments with %%%tau%%% protein. On reinvestigating this cross-reactivity we found that four of five mAbs to %%%phosphorylated%%% neurofilaments and four of five mAbs to nonphosphorylated neurofilaments failed to react with %%%tau%%% protein.
A fifth mAb (07-5) to %%%phosphorylated%%% neurofilament cross-reacted
with partially denatured %%%tau%%% protein at an affinity 1/1700th of that for denatured neurofilaments; nondenatured %%%tau%%% protein in tissue sections did not cross-react. A fifth mAb (02-40) to nonphosphorylated neurofilament also cross-reacted weakly. In %%%Alzheimer%%% disease normal-appearing axons were revealed with all the
mAbs to %%%phosphorylated%%% neurofilaments, but tangles were revealed
with only one of them (mAb 07-5). mAb to %%%tau%%% protein did not

stain
or did so indistinctly. Four of five mAbs to nonphosphorylated neurofilaments failed to reveal axons. Upon dephosphorylation of tissue, staining by mAbs to %%%phosphorylated%%% neurofilaments disappeared, and axons were revealed with the mAb to %%%tau%%% protein and all mAbs to the nonphosphorylated neurofilaments. Tangles became stained with %%%tau%%% mAb and one mAb to the nonphosphorylated neurofilaments (mAb 10-1). Quantitative evaluation of immunocytochemical staining intensities and immunoblot cross-reactivity showed that neurofilaments are, indeed, constituents of tangles-apparently exceeding the concentration of %%%tau%%% protein 17-fold. Contribution of both conformation and primary structure to IgG specificity may explain the lack of any cross-reaction of mAbs to neurofilaments with %%%tau%%% protein in intact tissue and the appearance of cross-reaction in immunoblots where conformation specificity may be largely lost. The present data extend earlier findings of abnormal processing of neurofilaments and %%%tau%%% protein in %%%Alzheimer%%% disease and, together with reported abnormal processing of cerebrovascular amyloid .beta.-protein, suggest that inhibition of the processing of multiple proteins is basic to the pathogenesis of %%%Alzheimer%%% disease, whereas formation of plaques and tangles could be merely the most striking histologic results.

8/7/114 (Item 114 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06847677 BIOSIS NO.: 000089006869
CHARACTERIZATION OF TWO PATHOLOGICAL %%%TAU%%% PROTEIN VARIANTS IN %%%ALZHEIMER%%% BRAIN CORTICES
AUTHOR: FLAMENT S; DELACOURTE A; HEMON B; DEFOSSEZ A
AUTHOR ADDRESS: INSERM UNITE NO. 16, LAB. NEUROSCI., FAC. MED. LILLE, F-59045 LILLE CEDEX, FR.
JOURNAL: J NEUROL SCI 92 (2-3). 1989. 133-142. %%%1989%%%
FULL JOURNAL NAME: Journal of the Neurological Sciences
CODEN: JNSCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% proteins were detected in brain tissue homogenates from 10 patients with %%%Alzheimer%%%'s disease versus 10 age-matched controls using the immunoblot technique and 2 polyclonal antibodies: anti-paired helical filaments (PHF) and anti-human native %%%Tau%%% proteins. In control brains, both antisera detected identically the normal set of %%%Tau%%% proteins, with molecular weight (MW) ranging from 45 to 62 kDa. Moreover, in association areas of neocortex from %%%Alzheimer%%% brains, the antisera detected 2 additional %%%Tau%%% variants of 64 and 69 kDa. %%%Tau%%% 64 and 69 were not found in regions of %%%alzheimer%%% brains where the %%%Alzheimer%%% pathology was absent (caudate nucleus or cerebellum for example). The heavy MW of %%%Tau%%% 64 and 69 is due to their %%%phosphorylation%%% state as shown by the decrease of their MW after alkaline phosphatase treatment. Therefore, %%%Tau%%% 64 and %%%Tau%%% 69 are specific markers of the %%%Alzheimer%%%'s disease neuronal degenerating process and their characterization demonstrates that an abnormal %%%phosphorylation%%% of %%%Tau%%% really occurs during the disease. %%%Tau%%% 64 and 69 were isolated with normal %%%Tau%%% proteins while the PHF were insoluble. Therefore, %%%Tau%%% proteins are likely to be abnormally %%%phosphorylated%%% prior to their incorporation in the PHF structure. Consequently, they might appear before the lesions and might be instrumental for the search of biochemical deregulations that precede the neurofibrillary degeneration.

8/7/115 (Item 115 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06778057 BIOSIS NO.: 000088087494
IDENTIFICATION AND LOCALIZATION OF A %%%TAU%%% PEPTIDE TO PAIRED HELICAL FILAMENTS OF %%%ALZHEIMER%%% DISEASE
AUTHOR: IQBAL K; GRUNDKE-IQBAL I; SMITH A J; GEORGE L; TUNG Y-C; ZAIDI T
AUTHOR ADDRESS: NEW YORK STATE INST. BASIC RES. DEVELOPMENTAL DISABILITIES, 1050 FOREST HILL RD., STATEN ISLAND, N.Y. 10314.
JOURNAL: PROC NATL ACAD SCI U S A 86 (14). 1989. 5646-5650. %%%1989%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Amino acid sequencing of a CNBr digest of the .%%%tau%%%. protein isolated from bovine brain revealed an amino acid sequence of 17 residues, Pro-Gly-Leu-Lys-Glu-Ser-Pro-Leu-Gln-Ile-Gly-Ala-Ala-Pro-Gly-Leu-Lys, which we call peptide I, with heterogeneity at position 11 of glycine (peptide Ia) and proline (peptide Ib); peptide I showed no homology with the previously reported cDNA-derived mouse and human .%%%tau%%%. sequences. Antisera raised to synthetic peptides corresponding to peptides Ia and Ib labeled all the bovine .%%%tau%%%. polypeptides recognized by other monoclonal and polyclonal antibodies to bovine . %%%tau%%%.. Antisera to peptide Ib did not label any mouse .%%%tau%%%. polypeptides; however, an anti-Ia antiserum labeled two of the four mouse .%%%tau%%%. polypeptides. Antisera to both peptides labeled paired helical filaments (PHF) as neurofibrillary tangles, plaque neurites, and neuropil threads in %%%Alzheimer%%% disease brain and PHF polypeptides on immunoblots. Immunostaining with anti-Ia antisera of PHF in tissue sections and PHF polypeptides, but not bovine .%%%tau%%%., on immunoblots was markedly increased when pretreated with alkaline phosphatase. These studies suggest that (i) the amino acid sequences of some isoforms of . %%%tau%%%. peptide might be different from that predicted from cDNAs, (ii) a .%%%tau%%%. peptide that is absent in the predicted sequences is present in PHF in %%%Alzheimer%%% disease, and (iii) .%%%tau%%%. in PHF is abnormally %%%phosphorylated%%%.

8/7/116 (Item 116 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06743025 BIOSIS NO.: 000088052455
BIOCHEMISTRY OF PAIRED HELICAL FILAMENTS PHF
AUTHOR: IHARA Y
AUTHOR ADDRESS: TOKYO METROPOLITAN INST. GERONTOL., JPN.
JOURNAL: JPN J GERIATR 25 (4). 1988. 364-367. %%%1988%%%
FULL JOURNAL NAME: Japanese Journal of Geriatrics
CODEN: NIRZA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: Since 1980, the nature of PHF has been heavily focused in several
laboratories. The most unexpected observation was that PHF are insoluble in harsh denaturants or detergents including SDS, urea and guanidine HCl. This unusual insolubility of PHF made possible high grade purification of PHF, but prevented the application of analytical biochemical methods to the identification of the PHF components. Therefore, we took an immunochemical approach using specific antibodies to PHF, which were prepared by immunization of purified PHF. Our strategy was to search for soluble polypeptides reactive with antiPHF, instead of analyzing PHF directly. Polyclonal antibodies to PHF were found to label %%%tau%%%, a neuron-specific microtubule-associated phosphoprotein. The analysis of PHF antisera showed that there are two populations of %%%tau%%% antibodies; one is reactive with both %%%phosphorylated%%% and nonphosphorylated forms of %%%tau%%%, the other is specific for %%%phosphorylated%%% %%%tau%%%. In addition, antibodies specific for
nonphosphorylated %%%tau%%% could not be detected in the PHF antisera.
From these observations, one of the antigenic determinants of PHF has been considered as %%%phosphorylated%%% %%%tau%%%. A hybridoma producing
a monoclonal antibody to PHF (DF2) was obtained by the fusion of mouse myeloma cells and rat spleen cells immunized with PHF. DF2 was confirmed to specifically bind to PHF. In the blot of the soluble fraction of brain homogenates, DF2 labeled a small polypeptide Mr .apprx. 5 kD, which was identified as ubiquitin by its purification and subsequent protein sequencing. Moreover, five ubiquitin fragments were identified in the PHF digest. Thus ubiquitin is a component of PHF. Two components, %%%tau%%%
and ubiquitin, have been identified in PHF immunochemically and protein chemically, respectively. Two lines of evidence suggest that PHF contain the components other than %%%tau%%% or ubiquitin: first, ghost tangles (extracellular tangles) are not stained with antiPHF or %%%tau%%% antibodies, although they appear to be made of PHF. Second, the staining activity of antiPHF cannot be absorbed out with excess amount of %%%tau%%%. These strongly suggest that PHF contain as-yet-unidentified components.

8/7/117 (Item 117 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06731501 BIOSIS NO.: 000088040928
THE PRESENCE OF %%%TAU%%% DISTINGUISHES LEWY BODIES OF DIFFUSE LEWY BODY
DISEASE FROM THOSE OF IDIOPATHIC PARKINSON DISEASE
AUTHOR: GALLOWAY P G; BERGERON C; PERRY G
AUTHOR ADDRESS: DEP. OF PATHOL., CHILD. HOSP. MED. CENT. OF AKRON, 281
LOCUST ST., AKRON, OHIO 44308, U.S.A.
JOURNAL: NEUROSCI LETT 100 (1-3). 1989. 6-10. %%%1989%%%
FULL JOURNAL NAME: Neuroscience Letters
CODEN: NELED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The antigenic components of Lewy bodies in the cerebral cortex and substantia nigra in 5 cases of diffuse Lewy body disease were examined by immunocytochemistry, using antibodies to neurofilaments (in the %%%phosphorylated%%% or non-%%%phosphorylated%%% forms); to ubiquitin; to the microtubule-associated proteins MAP1, MAP2 and %%%tau%%%; to isolated %%%Alzheimer%%% paired helical filaments, and to
tubulin, in the tyrosinated and non-tyrosinated forms. Immunoreactivity with antibodies to cytoskeletal components was identical to that previously described for Lewy bodies of idiopathic Parkinson disease, with the exception that the inclusions of diffuse Lewy body disease (in both cortex and substantia nigra) were stained by an antibody to %%%tau%%% protein. Our findings indicate that although the exclusions found in diffuse Lewy body disease share structural and epitopic features with the inclusions of idiopathic Parkinson disease, they also have distinguishing characteristics (in addition to the differing neuronal populations involved). Also, they suggest that although the inclusions in both conditions appear similar, they probably have different pathogenetic origins.

8/7/118 (Item 118 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06675461 BIOSIS NO.: 000087117638
SENILE PLAQUE NEURITES FAIL TO DEMONSTRATE ANTI-PAIRED HELICAL FILAMENT AND
ANTI-MICROTUBULE-ASSOCIATED PROTEIN-%%%TAU%%% IMMUNOREACTIVE PROTEINS IN
THE ABSENCE OF NEUROFIBRILLARY TANGLES IN THE NEOCORTEX
AUTHOR: PROBST A; ANDERTON B H; BRION J-P; ULRICH J
AUTHOR ADDRESS: DEP. PATHOL., DIV. NEUROPATHOL., UNIV. BASEL, SWITZERLAND.
JOURNAL: ACTA NEUROPATHOL 77 (4). 1989. 430-436. %%%1989%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Although much work has been directed recently towards unravelling
the protein chemistry of neurofibrillary tangle (NFT) and senile plaque (SP) components in %%%Alzheimer%%%'s disease, the pathogeneses of these
lesions remains largely unknown and the problem of their relationship is unresolved. In particular, although paired helical filaments (PHF) have long been documented in SP neurites, we do not know if they are of pathogenetic relevance for the formation of the SP. To investigate the relationship between NFT and SP, we examined antigenic properties of proteins in SP neurites in neocortical tissues of patients with senile dementia of %%%Alzheimer%%% type, in the presence or absence of NFT in
the same cortical area. We used two polyclonal antibodies directed against PHF and microtubule-associated protein (MAP)-%%%tau%%% and three
monoclonal antibodies (MAbs) (RT97, BF10, 147) to %%%phosphorylated%%%
epitopes of human neurofilament polypeptides, as well as the Gallyas silver impregnation method which specifically stains PHF in NFT and neurites. The main finding of our investigations consists in a differential pattern of immunoreactivity of SP neurites depending on the presence or absence of NFT in the neocortex. In the presence of NFT, there were numerous neuropil threads and SP neurites containing Gallyas-positive, as well as anti-PHF- and anti-%%%tau%%%-labelled material. In the absence of NFT in the neocortex there was a striking absence of any GAllyas-positive or PHF- and %%%tau%%%-immunoreactive structure in the cortical neuropil and in SP neurites, irrespective of the maturation stage of the SP. In contrast with these results, the number of neurites labelled by MAbs RT97, BF10 and 147 in SP and in the neuropil was apparently unaffected by the presence or absence of NFT. Amyloid in SP, remained consistently unstained by all antibodies of the panel as well as by the Gallyas stain. Our findings indicate that PHF and %%%tau%%% polypeptides are facultative components of SP neurites and suggest that the development of SP may occur independently of PHF pathology in neocortical neurons.

8/7/119 (Item 119 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06664050 BIOSIS NO.: 000087106227
IMMUNOCYTOCHEMICAL CHARACTERIZATION OF NEUROFIBRILLARY TANGLES IN
AMYOTROPIC LATERAL SCLEROSIS AND PARKINSONISM-DEMENTIA OF GUAM WEST
PACIFIC OCEAN
AUTHOR: SHANKAR S K; YANAGIHARA R; GARRUTO R M; GRUNDKE-IQBAL I; KOSIK K S;
GAJDUSEK D C
AUTHOR ADDRESS: NATL. INST. HEALTH, BUILD. 36, ROOM 5B-21, BETHESDA, MD
20892.

JOURNAL: ANN NEUROL 25 (2). 1989. 146-151. %%%1989%%%
FULL JOURNAL NAME: Annals of Neurology
CODEN: ANNED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Cryostat-cut sections of formalin-fixed and unfixed hippocampus
from 23 Guamanian Chamorros with clinically and neuropathologically verified amyotrophic lateral sclerosis (ALS) (8 cases) and parkinsonism-dementia (PD) (15 cases) and from 12 neurologically normal Guamanians (5 with and 7 without neurofibrillary degeneration) were evaluated by the immunoperoxidase technique, using monoclonal antibodies against %%%phosphorylated%%% neurofilament, human fetal microtubule-associated protein %%%tau%%%, and paired helical filaments. On immunostaining, all three antibodies showed intracellular tangles in the hippocampal neurons of patients with ALS, patients with PD, and in neurologically normal Guamanians with neurofibrillary pathology, but the correlation of immunostaining between these antibodies was not absolute. Extracellular or ghost tangles were immunostained only with the antibody against paired helical filaments. Our immunocytochemical data indicate that the antigenic composition of neurofibrillary tangles in Guamanian ALS and PD is similar to that of %%%Alzheimer%%%'s disease, suggesting a
common pathogenetic pathway for neurofibrillary tangle formation in these neurodegenerative disorders.

8/7/120 (Item 120 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06644905 BIOSIS NO.: 000087087082
ACCUMULATION OF ABNORMALLY %%%PHOSPHORYLATED%%% %%%TAU%%% PRECEDES THE
FORMATION OF NEUROFIBRILLARY TANGLES IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: BANCHER C; BRUNNER C; LASSMANN H; BUDKA H; JELLINGER K; WICHE G;
SEITELBERGER F; GRUNDKE-IQBAL I; IQBAL K; WISNIEWSKI H M
AUTHOR ADDRESS: INST. BASIC RES. DEVELOPMENTAL DISABILITIES, 1050 FOREST
HILL RD., STATEN ISLAND, N.Y. 10314, USA.
JOURNAL: BRAIN RES 477 (1-2). 1989. 90-99. %%%1989%%%
FULL JOURNAL NAME: Brain Research
CODEN: BRREA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The intraneuronal accumulation of paired helical filaments in the
form of neurofibrillary tangles is one hallmark of the brain pathology in %%%Alzheimer%%%'s disease. At certain predilection sites, a small number
of similar lesions are also present in the brains of the majority of aged non-demented individuals. As suggested by several studies before, these abnormal cytoskeletal structures contain determinants of microtubule-associated protein .%%%tau%%%. and ubiquitin. The present study uses a morphological classification of neurofibrillary tangles into different stages of maturation, as suggested by %%%Alzheimer%%% in 1911,
and shows by quantitative immunocytochemistry that early stages of neurofibrillary degeneration contain abnormally %%%phosphorylated%%% . %%%tau%%%.. Immunoreactivity for the altered .%%%tau%%%. is seen not only
in tangles but also in the cytoplasm of some nerve cells lacking neurons without tangles are present in age-matched non-demented individuals as in %%%Alzheimer%%% cases, but are absent in young controls. In contrast, incorporation of an epitope, recognized by a monoclonal antibody (3-39) raised to paired helical filaments, which is directed against a determinant residing in the 50-65 amino acid residue region of ubiquitin occurs late in the process of tangle maturation and is most pronounced in extracellular 'ghost tangles'. It is suggested that the accumulation of abnormally %%%phosphorylated%%% .%%%tau%%%. is one of the earliest cytoskeletal changes in the process of tangle formation. Exposure of certain ubiquitin epitopes in the pathological fibers may reflect an unsuccessful attempt of proteolytic degradation.

8/7/121 (Item 121 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06631242 BIOSIS NO.: 000087073404
PROGRESSIVE SUPRANUCLEAR PALSY EXTENSIVE NEUROPIL THREADS IN ADDITION TO
NEUROFIBRILLARY TANGLES VERY SIMILAR ANTIGENICITY OF SUBCORTICAL NEURONAL
PATHOLOGY IN PROGRESSIVE SUPRANUCLEAR PALSY AND %%%ALZHEIMER%%%'S DISEASE
AUTHOR: PROBST A; LANGUI D; LAUTENSCHLAGER C; ULRICH J; BRION J P; ANDERTON
B H
AUTHOR ADDRESS: DEP NEUROPATHOL., INST. PATHOL., UNIV. BASEL, SCHOEBEINSTRASSE 40, CH-4003 BASEL, SWITZ.
JOURNAL: ACTA NEUROPATHOL 77 (1). 1988. 61-68. %%%1988%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Light microscopic immunohistochemical investigations were performed on neurofibrillary tangles (NFT) in four histologically confirmed cases of %%%Alzheimer%%%'s disease (AD) and in five patients with a progressive supranuclear palsy (PSP). The antibody panel included antisera to the neuronal mirotubule-associated protein, %%%tau%%%, and to
isolated paired helical filaments (PHF), as well as mouse monoclonal antibodies (MAbs) to %%%phosphorylated%%% epitopes on high and medium
molecular weight neurofilament subunits (RT97 and BF10, respectively). Paraffin sections were also impregnated with the Gallyas silver method, which specifically stains tangles and cortical neuropil threads in AD, but does not stain normal neurofilaments. All tangles in PSP and AD showed consistent immunostaining with antibodies to %%%tau%%% protein and
isolated PHF, regardless of their localization. MAbs RT97 and BF10, however, did not stain or only weakly stained, subcortical tangles in PSP and AD, whereas most cortical NFT in AD were intensely immunostained. All
tangles In PSP were as heavily impregnated with Gallyas as they were in AD. Furthermore there were extensive networks of Gallyas-positive, %%%tau%%%- and PHF-immunoreactive neurites in subcortical gray areas containing NFT, and bundles of positive axons in white matter tracts interconnecting subcortical nuclei of PSP. Our studies indicate a much more extensive disruption of fibrillar proteins in PSP subcortical neurons than previously reported. They furthermore indicate a very similar antigenic profile of NFT in PSP and AD, as far as subcortical neurons are concerned.

8/7/122 (Item 122 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06608948 BIOSIS NO.: 000087051110
SIMILARITIES AND DIFFERENCES BETWEEN %%%TAU%%% PROTEIN AND CHROMOBINDIN A
AUTHOR: STERNBERG H; BAUDIER J; AKIZUKI K; COLE G M; MARTIN W H; CREUTZ C E
; TIMIRAS P S; COLE R D
AUTHOR ADDRESS: DEP. PHYSIOLOGY-ANAT., UNIV. CALIF., BERKELEY, CALIF.
94720.
JOURNAL: NEUROCHEM INT 13 (2). 1988. 149-152. %%%1988%%%
FULL JOURNAL NAME: Neurochemistry International
CODEN: NEUID
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: %%%Tau%%% protein and Chromobindin A have several features in

common but are not identical. Both consist of a small group of closely related proteins which can form aggregates. Both have a similar range of molecular weights (53-62 kDa) and isoelectric points of (6.0-7.5). While Chromobindin a is known to be membrane associated, there is evidence that %%%Tau%%% protein also interacts with phospholipids. Both, not present in
all tissues, can be found in the adrenal medulla. Despite these similarities both classes of proteins are unique and immunologically distinct. A rabbit antisera to %%%Tau%%% does not cross react with Chromobindin A. In addition, while protein kinase C and Ca/Calmodulin-dependent protein kinase II %%%phosphorylate%%% %%%Tau%%% potein, they do not %%%phosphorylate%%% Chromobindin A, demonstrating the specificity of these kinases for %%%Tau%%% protein %%%phosphorylation%%%.

8/7/123 (Item 123 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06576823 BIOSIS NO.: 000087018984
A NOVEL TUBULIN-DEPENDENT PROTEIN KINASE FORMING A PAIRED HELICAL FILAMENT EPITOPE ON %%%TAU%%%
AUTHOR: ISHIGURO K; IHARA Y; UCHIDA T; IMAHORI K
AUTHOR ADDRESS: MITSUBISHIKASEI INST. LIFE SCI., MACHIDA, TOKYO 194.
JOURNAL: J BIOCHEM (TOKYO) 104 (3). 1988. 319-321. %%%1988%%%
FULL JOURNAL NAME: Journal of Biochemistry (Tokyo)
CODEN: JOBIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: From rat brain microtubule proteins, we purified a protein kinase that %%%phosphorylated%%% %%%tau%%%, one of microtubule-associated proteins. The electrophoretic mobility of the %%%phosphorylated%%% %%%tau%%% on SDS-polyacrylamide gel decreased. The enzyme was not activated by cyclic nucleotides, calmodulin, or phospholipids, and was inhibited by the calcium ions. The kinase bound to %%%tau%%%. The %%%phosphorylation%%% of %%%tau%%% was stimulated by tubulin under the coinditions of microtubule formation. From these results we propose an idea that the %%%phosphorylation%%% could occur concomitantly with microtubule formation in the brain. Human %%%tau%%% %%%phosphorylated%%% by the kinase carried an epitope of the paired helical filaments that accumulate in the brain in %%%Alzheimer%%%'s disease.

8/7/124 (Item 124 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06565676 BIOSIS NO.: 000087007837
NEUROFIBRILLARY TANGLES AND SENILE PLAQUES IN AGED BEARS
AUTHOR: CORK L C; POWERS R E; SELKOE D J; DAVIES P; GEYER J J; PRICE D L
AUTHOR ADDRESS: NEUROPATHOL. LAB., 509 PATHOL. BUILDING, JOHNS HOPKINS UNIV. SCH. MED., 600 NORTH WOLFE ST., BALTIMORE, MD. 21205-2182.
JOURNAL: J NEUROPATHOL EXP NEUROL 47 (6). 1988. 629-641. %%%1988%%%
FULL JOURNAL NAME: Journal of Neuropathology & Experimental Neurology
CODEN: JNENA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In aged human beings and in individuals with age-associated degenerative disorders, particularly %%%Alzheimer%%%'s disease (AD), neurons develop cytoskeletal abnormalities, including neurofibrillary tangles (NFT) and senile plaques (SP). Senile plaques occur in several nonhuman species; however, NFT, with ultrastructural or immunocytochemical similarities to those occurring in humans, have not been identified in other mammals. In this study of five aged bears (Ursus, 20-30 years of age), we identified cytoskeletal abnormalities similar to those occurring in humans. An aged Asiatic brown bear had NFT, composed of straight 10-16-nm filaments, that were immunoreactive with antibodies directed against: %%%phosphorylated%%% epitopes of neurofilaments (NF); %%%tau%%%; A68 (a protein enriched in AD); and an antigen associated with paired helical filaments (PHF). An aged polar bear had numerous SP; neurites of these plaques were immunoreactive with antibodies against %%%phosphorylated%%% epitopes of NF, but NFT were not identified. These results indicate that nonprimate species develope age-related cytoskeletal abnormalities similar to those occurring in humans. Investigations of the comparative pathology of aged mammals may be useful in elucidating the pathogeneses of these abnormalities.

8/7/125 (Item 125 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06565581 BIOSIS NO.: 000087007742
%%%ALZHEIMER%%% DISEASE TANGLES SHARE IMMUNOLOGICAL SIMILARITIES WITH MULTIPHOSPHORYLATION REPEATS IN THE TWO LARGE NEUROFILAMENT PROTEINS
AUTHOR: LEE V M-Y; OTVOS L JR; SCHMIDT M L; TROJANOWSKI J Q
AUTHOR ADDRESS: DEP. PATHOL., LAB. MED., UNIV. PENNSYLVANIA SCH. MED., PHILADELPHIA, PA. 10104.
JOURNAL: PROC NATL ACAD SCI U S A 85 (19). 1988. 7384-7388. %%%1988%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Immunological and structural analyses of neurofilament (NF) proteins with > 500 anti-NF monoclonal antibodies (mAbs) enumerated epitopes shared by NF proteins and %%%Alzheimer%%% neurofibrillary tangles. We identified the multiphosphorylation domain of the rat heaviest NF subunit-tandem repeats of Lys-Ser-Pro-Xaa (where Xaa is a small uncharged amino acid and serine is %%%phosphorylated%%%)-as the determinant recognized by 15 of the 16 mAbs from this collection of > 500 mAbs that detected neurofibrillary tangles. Most (11) of these 16 mAbs also recognized the previously characterized multiphosphorylation repeat in the human middle sized NF subunit. However, although these mAbs shared the ability to recognize NFTs, the antigen-binding domains of these 16 mAbs represented 13 separate classes based on their differential recognition of 12 synthetic peptides derived from the rat heaviest NF subunit and the human middle-sized NF subunit multiphosphorylation sites, NF subunits of 10 diverse species, and normal human .%%%tau%%%. protein.
We conclude that NFTs share highly specific immunological and structural properties with specific rat heaviest NF subunit and human middle-sized NF subunit multiphosphorylation repeats.

8/7/126 (Item 126 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06361347 BIOSIS NO.: 000036064500
CURRENT HYPOTHESES OF %%%ALZHEIMER%%% DISEASE NEUROPATHOLOGY AND DEMENTIA
AUTHOR: WISNIEWSKI H M; MERZ G S; RABE A; BARCIKOWSKA M; MORETZ R C; DEVINE-GAGE E A
AUTHOR ADDRESS: INST. BASIC RES. DEV. DISABILITIES, 1050 FOREST HILL ROAD,

STATEN ISLAND, N.Y. 10314.
JOURNAL: SYMPOSIUM ON IMMUNE DYSFUNCTIONS: NEW TARGETS OF DRUG DISCOVERY
FOR ALZHEIMER'S DISEASE AND OTHER COGNITIVE DISORDERS HELD AT THE 17TH
ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, NEW ORLEANS, LOUISIANA,
USA, NOVEMBER 16, 1987. DRUG DEV RES 15 (2-3). 1988. 115-122. %%%1988%%%
CODEN: DDRED
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/127 (Item 127 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06326720 BIOSIS NO.: 000036029873
LEUPEPTIN CAUSES AN ACCUMULATION OF %%%PHOSPHORYLATED%%% %%%TAU%%% AND UBIQUITIN IN RAT BRAIN
AUTHOR: IVY G O; KITANI K; IHARA Y
AUTHOR ADDRESS: LIFE SCI., UNIV. TORONTO, TORONTO, ONT. M1C 1A4.
JOURNAL: 18TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, TORONTO,
ONTARIO, CANADA, NOVEMBER 13-18, 1988. SOC NEUROSCI ABSTR 14 (2). 1988.
1291. %%%1988%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/128 (Item 128 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06271069 BIOSIS NO.: 000086105252
ANTIGENIC CHARACTERISTICS OF NEUROFIBRILLARY TANGLES IN PROGRESSIVE SUPRANUCLEAR PALSY
AUTHOR: GALLOWAY P G
AUTHOR ADDRESS: CLEVELAND METROPOLITAN GENERAL HOSP., DEP. PATHOL., 3395 SCRANTON ROAD, CLEVELAND, OHIO 44109, USA.
JOURNAL: NEUROSCI LETT 91 (2). 1988. 148-153. %%%1988%%%
FULL JOURNAL NAME: Neuroscience Letters
CODEN: NELED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The antigenic components of neurofibrillary tangles in the basal forebrain and brainstem were studied in 4 cases of progressive supranuclear palsy (PSP) at the light and electron microscopic levels, using antibodies to neurofilaments (in the %%%phosphorylated%%% and non-%%%phosphorylated%%% forms); the high, middle and low molecular weight neurofilament subunits; ubiquitin; the microtubule associated proteins MAP1, MAP2 and %%%tau%%%; isolated %%%Alzheimer%%% paired helical filaments and to tubulin, in the tyrosinated and detyrosinated forms. Although PSP neurofibrillary tangles appear to have most antigenic sites in common with those of %%%Alzheimer%%% disease, PSP tangles share epitopes with tyrosinated and detyrosinated tubulin, which has not been demonstrated in %%%Alzheimer%%% neurofibrillary tangles.

8/7/129 (Item 129 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06260275 BIOSIS NO.: 000086094458
MICROTUBLE-ASSOCIATED POLYPEPTIDES %%%TAU%%% ARE ALTERED IN %%%ALZHEIMER%%% PAIRED HELICAL FILAMENTS
AUTHOR: GRUNDKE-IQBAL I; VORBRODT A W; IQBAL K; TUNG Y-C; WANG G P; WISNIEWSKI H M
AUTHOR ADDRESS: NYS INST. BASIC RES. DEVELOPMENTAL DISABILITIES, 1050 FOREST HILL ROAD, STATEN ISLAND, N.Y. 10314.
JOURNAL: MOL BRAIN RES 4 (1). 1988. 43-52. %%%1988%%%
FULL JOURNAL NAME: Molecular Brain Research
CODEN: MBREE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Antisera were raised in rabbits to purified bovine %%%tau%%% and to isolated %%%Alzheimer%%% paired helical filaments (PHF) washed with sodium dodecyl sulfate (SDS). Both anti-%%%tau%%% and anti-PHF sera labeled at electron microscopic level PHF which has been isolated either by extraction with SDS or treatment with crude collagenase. On immunoblots all anti-%%%tau%%% and anti-PHF sera labeled bovine brain %%%tau%%% as well as the major 45-to 62-kDa PHF polypeptides which had been previously shown to co-migrate on SDS gels with normal human %%%tau%%% (J. Biol. Chem., 261 (1986) 6084-6089). All antisera labeled %%%Alzheimer%%% neurofibrillary tangles on tissue sections and the PHF polypeptides on immunoblots. Pretreatment with alkaline phosphatase had no effect on the immunostaining. The antisera did not react with ubiquitin, neurofilament triplet polypeptides and with the exception of one antiserum with tubulin and high-molecular weight microtubule-associated proteins. Absorption of %%%tau%%% antisera with %%%tau%%% and PHF and of PHF antisera with PHF resulted in complete removal of the tangles-staining antibodies. In case of the anti-PHF sera when absorbed with %%%tau%%%, only staining of a certain tangles population, the dense type, was eliminated and that too at more than 20 times the amount needed for the anti-%%%tau%%% sera; the staining of the loosely packed type of tangles, presumably the final stage, gradually decreased but was not completely abolished. On immunoblots the %%%tau%%% -like major PHF bands remained labeled by the %%%tau%%%-absorbed anti-PHF sera. These studies indicate that %%%tau%%% in PHF is present in different states of modification and that these alterations in %%%tau%%% are in addition to the abnormal %%%phosphorylation%%% shown previously.

8/7/130 (Item 130 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06216596 BIOSIS NO.: 000086050778
PHOSPHORUS-31 NMR STUDY OF THE BRAIN IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: PETTEGREW J W; MOOSSY J; WITHERS G; MCKEAG D; PANCHALINGAM K
AUTHOR ADDRESS: LAB. NEUROPHYSICS, DEP. PSYCHIATRY AND NEUROL., UNIV. PITTSBURGH, WESTERN PSYCHIATRIC INST. AND CLINIC, 3811 O'HARA ST., PITTSBURGH, PA. 15213.
JOURNAL: J NEUROPATHOL EXP NEUROL 47 (3). 1988. 235-248. %%%1988%%%
FULL JOURNAL NAME: Journal of Neuropathology & Experimental Neurology
CODEN: JNENA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The histopathological hallmarks of %%%Alzheimer%%%'s disease have long been considered to be neurofibrillary tangles (NFT) and neuritic (senile) plaques (SP). Neither of these structures, however, are unique to %%%Alzheimer%%%'s disease, and both probably represent end-stage

markers of the disorder. NFT have been demonstrated in many disorders; SP
occur in small numbers with normal aging. Evidence is presented for elevation of phosphomonoesters (PME) in %%%Alzheimer%%%'s brain compared to non-%%%Alzheimer%%%'s diseased controls and normal controls. The PME detected by 31P nuclear magnetic resonance (NMR) spectroscopy of autopsy brain are predominantly anabolic precursors of membrane phospholipids. Elevated PME could be secondary to a metabolic block at the rate-limiting enzyme in membrane phospholipid synthesis, which is cytidine triphosphate (CTP):phosphocholine (or phosphoethanolamine)cytidyltransferase (EC 2.7.7.15). Elevated PME could also be secondary to decreased breakdown of PME by phospholipase D activity. Since CTP:phosphocholine cytidyltransferase is inactivated by %%%phosphorylation%%% and since there is independent evidence for hyperphosphorylation of %%%tau%%% and MAP-2 proteins in AD brain, enhanced protein kinase activity could be a common factor. Preliminary evidence suggests that PME could interact with N-methyl-D-aspartate receptors and potentially act as false neurotransmitters. Further studies will be needed to investigate these possibilities.

8/7/131 (Item 131 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06151013 BIOSIS NO.: 000085114165
IDENTIFICATION OF THE MAJOR MULTIPHOSPHORYLATION SITE IN MAMMALIAN NEUROFILAMENTS
AUTHOR: LEE V M-Y; OTVOS L JR; CARDEN M J; HOLLOSI M; DIETZSCHOLD B; LAZZARINI R A
AUTHOR ADDRESS: DIV. NEUROPATHOL., DEP. PATHOL. LAB. MED., UNIV. PA. SCH. MED., PHILADELPHIA, PA. 19104.
JOURNAL: PROC NATL ACAD SCI U S A 85 (6). 1988. 1998-2002. %%%1988%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The sequence Lys-Ser-Pro-Val-Pro-Lys-Ser-Pro-Val-Glu-Glu-Lys-Gly repeats six times serially in the human midsized neurofilament (NF) protein (NF-M). To establish whether Lys-Ser-Pro-Val(Ala) is the major site for in vivo NF %%%phosphorylation%%%, peptides based on the human NF-M repeat were synthesized and chemically %%%phosphorylated%%%. These synthetic peptides were probed with 515 monoclonal antibodies (mAbs) that wereraised to, and distinguished, several differentially %%%phosphorylated%%% forms of NF proteins. Studies with 95 of those mAbs that recognized the peptides before and after chemical %%%phosphorylation%%% demonstrated that a highly immunogenic epitope shared by the peptides is present in NFs from all species tested, including invertebrates. This suggests the phylogenetic conservation of a major NF %%%phosphorylation%%% site. Lastly, a cross-reactive antigenic determinant shared by the petpides and the major NF %%%phosphorylation%%% site was shown to exist in neurofibrillary tangles of patients with %%%Alzheimer%%% disease as well as in two neuron-specific microtubule-associated proteins (MAPs).sbd.i.e., MAP2 and %%%tau%%%.

8/7/132 (Item 132 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06097112 BIOSIS NO.: 000085060261
%%%PHOSPHORYLATION%%% OF %%%TAU%%% PROTEINS TO A STATE LIKE THAT IN %%%ALZHEIMER%%%'S BRAIN IS CATALYZED BY A CALCIUM-CALMODULIN-DEPENDENT KINASE AND MODULATED BY PHOSPHOLIPIDS
AUTHOR: BAUDIER J; COLE R D
AUTHOR ADDRESS: DEP. BIOCHEM., UNIV. CALIFORNIA, BERKELEY, CALIF. 94720.
JOURNAL: J BIOL CHEM 262 (36). 1987. 17577-17583. %%%1987%%%
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Calcium/calmodulin (CaM)-dependent protein kinases isolated from bovine and rat brains %%%phosphorylate%%% the microtubule-associated %%%tau%%% protein in the mode that shifts the mobility of %%%tau%%% in sodium dodecyl sulfate-polyacrylamide gel electrophoresis (mode 1). This mode of %%%tau%%% %%%phosphorylation%%% is the one that occurs abnormally in %%%Alzheimer%%%'s lesions. Purified %%%tau%%% protein in solution can be %%%phosphorylated%%% by the Ca2+/CaM kinases maximally to about 50% of the total %%%tau%%% protein. Incorporation of one phosphate group per mol of %%%tau%%% is sufficient to shift the protein to a slower migrating electrophoretic band. Additional phosphate incorporation into the shifted %%%tau%%% proteins can occur depending on protein kinase concentration. In the presence of phosphatidylserine, %%%tau%%% proteins were %%%phosphorylated%%% to an extent of 100% at a %%%tau%%% :phosphatidylserine ratio of 20. Phosphatidylethanolamine also stimulated %%%tau%%% %%%phosphorylation%%% by Ca2+/CAM kinase and phosphatidylinositol was found to be a potent inhibitor of %%%tau%%% protein phoshorylation. The direct observation that %%%tau%%% proteins interact with phospholipids such as phosphatidylethanolamine and phosphatidylinositol, resulting in a smearing of the protein band on sodium dodecyl sulfate-gel electrophoresis, supports the possibility that two %%%tau%%% protein may interact with phospholipid membranes in vivo and that %%%tau%%% protein %%%phosphorylation%%% could be modulated by the phospholipid composition of the membranes with which %%%tau%%% interacts.

8/7/133 (Item 133 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05733122 BIOSIS NO.: 000084081528
NEUROFIBRILLARY TANGLES IN %%%ALZHEIMER%%%'S DISEASE AND PROGRESSIVE SUPRANUCLEAR PALSY ANTIGENIC SIMILARITIES AND DIFFERENCES
MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% ANTIGENICITY IS PROMINENT IN ALL TYPES OF TANGLES
AUTHOR: BANCHER C; LASSMANN H; BUDKA H; GRUNDKE-IQBAL I; IQBAL K; WICHE G; SEITELBERGER F; WISNIEWSKI H M
AUTHOR ADDRESS: NEUROL. INST., UNIV. VIENNA, SCHWARZSPANIERSTRASSE 17, A-1090 WIEN, AUSTRIA.
JOURNAL: ACTA NEUROPATHOL 74 (1). 1987. 39-46. %%%1987%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The antigenic profile of neurofibrillary tangles (NFT) in %%%Alzheimer%%%'s disease (AD), senile dementia of %%%Alzheimer%%% type (SDAT), progressive supranuclear palsy (PSP) and in non-demented aged

humans was investigated by light and electron microscopic immunocytochemistry using antisera and monoclonal antibodies to tubulin, microtobule-associated proteins (MAP1, MAP2 and %%%tau%%%), neurofilament proteins and determinants unique to %%%Alzheimer%%% paired helical filaments (PHF). Antibodies to %%%tau%%% proteins labeled NFT in all cases investigated (AD, SDAT, PSP and non-demented aged humans). However, one monoclonal antibody to PHF recognized numerous tangles in AD/SDAT, but only a small minority of the PSP tangles. Antibodies to tubulin, MAP1, MAP2 and neurofilament proteins did not selectively stain NFT. Whereas pretreatment of sections with phosphatase was required for the detection of tangles with %%%Tau%%%-1 monoclonal antibody, digestion of sections with either phosphatase or pronase had no significant effect on the staining pattern obtained with the other antibodies. Our studies show that, as previously described for AD/SDAT, %%%phosphorylated%%% %%%tau%%% polypeptides are also a major antigenic determinant of tangles in PSP, indicating that tangle formation may follow a common pathogenetic pathway in neurofibrillary degenerations. There is, however at least one epitope in AD/SDAT tangles which seems to be absent on, or at least inaccessible in the 15-nm straight fibrils of PSP.

8/7/134 (Item 134 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05702307 BIOSIS NO.: 000084050712
A MONOCLONAL ANTIBODY THAT RECOGNIZES A %%%PHOSPHORYLATED%%% EPITOPE IN %%%ALZHEIMER%%% NEUROFIBRILLARY TANGLES NEUROFILAMENTS AND %%%TAU%%% PROTEINS IMMUNOSTAINS GRANULOVACUOLAR DEGENERATION
AUTHOR: DICKSON D W; KSIEZAK-REDING H; DAVIES P; YEN S-H
AUTHOR ADDRESS: DEP. PATHOL., ALBERT EINSTEIN COLL. MED., 1300 MORRIS PARK AVE., K-438, BRONX, NY 10461, USA.
JOURNAL: ACTA NEUROPATHOL 73 (3). 1987. 254-258. %%%1987%%%
FULL JOURNAL NAME: Acta Neuropathologica
CODEN: ANPTA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A monoclonal antibody, raised against extracts from %%%Alzheimer%%% brain, that recognizes a %%%phosphorylated%%% epitope in high molecular weight neurofilament proteins and %%%tau%%% proteins also immunostains %%%Alzheimer%%% neurofibrillary tangles, neurites in senile plaques and granulovacuolar degeneration. This result suggests that granulovacuolar degeneration may contain %%%phosphorylated%%% proteins, possibly due to autophagy of %%%phosphorylated%%% perikaryal proteins that appear to be increased in %%%Alzheimer%%%'s disease.

8/7/135 (Item 135 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05700178 BIOSIS NO.: 000084048583
RECOGNITION OF %%%ALZHEIMER%%% PAIRED HELICAL FILAMENTS BY MONOCLONAL NEUROFILAMENT ANTIBODIES IS DUE TO CROSSREACTION WITH %%%TAU%%% PROTEIN
AUTHOR: NUKINA N; KOSIK K S; SELKOE D J
AUTHOR ADDRESS: HARVARD MED. SCH., CENT. NEUROL. DISEASES, DEP. MED., 75 FRANCIS ST., BOSTON, MASS. 02115.
JOURNAL: PROC NATL ACAD SCI U S A 84 (10). 1987. 3415-3419. %%%1987%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Neurofibrillary tangles and senile plaques are the principal pathological features of %%%Alzheimer%%% disease. Neurofibrillary tangles and the neurites of senile plaques contain paired helical filaments (PHF) that consist of two 10-nm filaments twisted into a double helix. The precursor proteins of PHF are not fully known. To identify these precursors, numerous immunochemical studies have been carried out during the past decade. Two apparently conflicting results have been reported. (i) Some, but not all, monoclonal antibodies to neurofilaments stained neurofibrillary tangle. (ii) Polyclonal antibodies prepared to PHF purified in NaDodSO4 because of their unusual insolubility did not recognize normal proteins, including neurofilaments, on electrophoretic transfer blots of human brain homogenates. These results have been confirmed in several laboratories, including by the use of electron microscopic labeling. Recently, we reported that polyclonal PHF antibodies include antibodies to %%%tau%%% proteins, a family of heat-stable microtubule-associated phosphoproteins, and that antibodies to %%%tau%%% stain %%%Alzheimer%%% neurofibrillary tangles. Those monoclonal neurofilament antibodies that recognize tangles are reported to be directed against %%%phosphorylated%%% epitopes. These facts prompted us to reexamine certain neurofilament monoclonal antibodies that stain neurofibrillary tangles. All monoclonal neurofilament antibodies that stain tangles that we examined, including those initially reported, reacted with %%%tau%%% proteins. Our results suggest that these antibodies react with %%%phosphorylated%%% %%%tau%%% proteins in PHF, not neurofilament proteins, highlighting the problem of using antibodies to %%%phosphorylated%%% protein epitopes in immunochemical studies. Independent evidence for the presence of neurofilament proteins in human paired helical filaments is now required.

8/7/136 (Item 136 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05604691 BIOSIS NO.: 000083077831
TWO MONOCLONAL ANTIBODIES RECOGNIZE %%%ALZHEIMER%%%'S NEUROFIBRILLARY TANGLES NEUROFILAMENT AND MICROTUBULE-ASSOCIATED PROTEINS
AUTHOR: KSIEZAK-REDING H; YEN S-H
AUTHOR ADDRESS: DEP. OF PATHOL. FORCH. 538 , ALBERT EINSTEIN COLL. OF MED., 1300 MORRIS PARK AVE., BRONX, NY 10461, USA.
JOURNAL: J NEUROCHEM 48 (2). 1987. 455-462. %%%1987%%%
FULL JOURNAL NAME: Journal of Neurochemistry
CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Two monoclonal antibodies that recognize %%%Alzheimer%%%'s neurofibrillary tangles (ANTs), AD10 and AB18, have been characterized by immunoblotting against human and calf spinal cord neurofilament (NF) and calf brain microtubule preparations. Both antibodies bind to the 200-kilodalton (kd) (NF-H) and 160-kd (NF-M) but not to the 68-kd (NF-L) NF triplet proteins. They also bind to high-molecular-weight microtubule-associated proteins (MAPs) and .%%%tau%%%..AD10 immunostains MAP2 and MAP1 families, whereas AB18 stains mainly MAP1 bands. Preincubation of intact filament preparation or nitrocellulose strips containing electroblotted NF proteins with Escherichia coli alkaline phosphatase completely blocks AD10 binding and partially blocks binding of AB18. These results suggest that the determinants recognized by these antibodies are %%%phosphorylated%%%. Immunoblotting of peptide fragments generated by limited proteolysis of NF proteins with .alpha.-chymotrypsin and Staphylococcus aureus V8 protease shows that the localization of the antigenic determinants to AD10 and AB18 in NF-H is .apprx. 100 and 60 kd, respectively, away from the carboxy terminal, a region previously shown

to form the NF projection side arm. In NF-M, the antigenic determinants to both antibodies are located also in the projection side arm, in a 60-kd polypeptide adjacent to the .alpha.-helical filament core. The results show that ANTs contain at least two %%%phosphorylated%%% antigenic sites that are present in NF and MAPs, a finding suggesting that ANTs may be composed of proteins or their fragments with epitopes shared by cytoskeletal proteins.

8/7/137 (Item 137 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05484350 BIOSIS NO.: 000033085203
MICROTUBULE ASSOCIATED PROTEIN %%%TAU%%% IN %%%ALZHEIMER%%% PAIRED HELICAL
FILAMENTS PHF
AUTHOR: IQBAL K; GRUNDKE-IQBAL I; WISNIEWSKI H M
AUTHOR ADDRESS: INST. BASIC RES. DEV. DISABILITIES, STATEN ISLAND, N.Y.
10314, USA.
JOURNAL: ELEVENTH MEETING OF THE INTERNATIONAL SOCIETY FOR NEUROCHEMISTRY
AND THE EIGHTEENTH MEETING OF THE AMERICAN SOCIETY FOR NEUROCHEMISTRY, LA
GUAIRA, VENEZUELA, MAY 31-JUNE 5, 1987. J NEUROCHEM 48 (SUPPL.). 1987.
S157. %%%1987%%%
CODEN: JONRA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/138 (Item 138 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05263909 BIOSIS NO.: 000082104534
DEFECTIVE BRAIN MICROTUBULE ASSEMBLY IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: IQBAL K; GRUNDKE-IQBAL I; ZAIDI T; MERZ P A; WEN G Y; SHAIKH S S;
WISNIEWSKI H M; ALAFUZOFF I; WINBLAD B
AUTHOR ADDRESS: NYS INST. BASIC RES. DEV. DISABILITIES, 1050 FOREST HILL
ROAD, STATEN ISLAND, NEW YORK 10314, USA.
JOURNAL: LANCET 2 (8504). 1986. 421-426. %%%1986%%%
FULL JOURNAL NAME: Lancet
CODEN: LANCA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Brains obtained within 2-4 hours post mortem and histopathologically confirmed for %%%Alzheimer%%%'s disease and non-%%%Alzheimer%%% brains from age-matched controls were examined for in-vitro assembly of microtubules and neurofilaments. Microtubule assembly was observed only in control but not in %%%Alzheimer%%% brains, and neurofilaments were obained from both types of brain. The microtubule-associated protein %%%tau%%%, which stimulates assembly for microtubules from tubulin, was abnormally %%%phosphorylated%%% in %%%Alzheimer%%% but not in control brain microtubule preparations. %%%Alzheimer%%% brains did not show the presence of any inhibitor of microtubule assembly or any abnormality of tubulin. DEAE-dextran, a polycation which mimics %%%tau%%% in stimulating microtubule assembly, induced the assembly of microtubules in %%%Alzheimer%%% brain. Tubulin from both normal and %%%Alzheimer%%% brains was labelled on western blots by a monoclonal antibody to the tyrosinylated carboxy-terminal epitope of .alpha. tubulin. These studies suggest that in %%%Alzheimer%%%'s disease tubulin can be assembled into brain microtubules, but the process is defective, probably because of abnormal %%%phosphorylation%%% of %%%tau%%%. This post-translational alteration of %%%tau%%% might be the cause of the neurofibrillary abnormality in %%%Alzheimer%%%'s disease.

8/7/139 (Item 139 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05244550 BIOSIS NO.: 000082085172
%%%PHOSPHORYLATED%%% %%%TAU%%% PROTEIN IS INTEGRATED INTO PAIRED HELICAL
FILAMENTS IN %%%ALZHEIMER%%%'S DISEASE
AUTHOR: IHARA Y; NUKINA N; MIURA R; OGAWARA M
AUTHOR ADDRESS: TOKYO METROPOLITAN INST. GERONTOL., ITABASHI-KU, TOKYO 173.
JOURNAL: J BIOCHEM (TOKYO) 99 (6). 1986. 1807-1810. %%%1986%%%
FULL JOURNAL NAME: Journal of Biochemistry (Tokyo)
CODEN: JOBIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Antisera to paired helical filaments (PHF) were found to contain a significant amount of %%%tau%%% antibodies specific for a %%%phosphorylated%%% form, but only a negligible amount of those specific for a non-%%%phosphorylated%%% form. Also, the %%%phosphorylated%%% %%%tau%%%-specific antibodies, but not the non-%%%phosphorylated%%% %%%tau%%%-specific ones, labeled neurofibrillary tangles isolated in the presence of sodium dodecyl sulfate (SDS) and stained both tangles and senile plaque neurites in fixed tissue sections in a very similar way to as the whole antiserum did. Taken together, these results strongly suggest that a major antigenic determinant of PHF is %%%phosphorylated%%% %%%tau%%% itself.

8/7/140 (Item 140 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05234674 BIOSIS NO.: 000082075296
ABNORMAL %%%PHOSPHORYLATION%%% OF THE MICROTUBULE-ASSOCIATED PROTEIN
%%%TAU%%% IN %%%ALZHEIMER%%% CYTOSKELETAL PATHOLOGY
AUTHOR: GRUNDKE-IQBAL I; IQBAL K; TUNG Y-C; QUINLAN M; WISNIEWSKI H M;
BINDER L I
AUTHOR ADDRESS: N.Y. STATE UNIV. BASIC RES. DEV. DISABILITIES, 1050 FOREST
HILL ROAD, STATEN ISLAND, N.Y. 10314.
JOURNAL: PROC NATL ACAD SCI U S A 83 (13). 1986. 4913-4917. %%%1986%%%
FULL JOURNAL NAME: Proceedings of the National Academy of Sciences of the
United States of America
CODEN: PNASA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A monoclonal antibody to the microtubule-associated protein . %%%tau%%%. (%%%tau%%%) labeled some neurofibrillary tangles and plaque neurites, the two major locations of paired-helical filaments (PHF), in %%%Alzheimer%%% disease brain. The antibody also labeled isolated PHF that had been repeatedly washed with NaDodSO4. Dephosphorylation of the tissue sections with alkaline phosphatase prior to immunolabeling dramatically increased the number of tangles and plaques recognized by the antibody. The plaque core amyloid was not stained in either dephosphorylated or nondephosphorylated tissue sections. On immunoblots PHF polypeptides were labeled readily only when dephosphorylated. In contrast, a commercially available monoclonal antibody to a %%%phosphorylated%%% epitope of neurofilaments that labeled the tangles and the plaque neurites in tissue did not label any PHF polypeptides on

immunoblots. The PHF polypeptides, labeled with the monoclonal antibody to .%%%tau%%%., electrophoresed with those polypeptides recognized by antibodies to isolated PHF. The antibody to .%%%tau%%%.-labeled microtubules from normal human brains assembled in vitro but identically treated %%%Alzheimer%%% brain preparations had to be dephosphorylated to
be completely recognized by this antibody. These findings suggest that . %%%tau%%%. in %%%Alzheimer%%% brain is an abnormally %%%phosphorylated%%%
protein component of PHF.

8/7/141 (Item 141 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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05031296 BIOSIS NO.: 000031106428
%%%ALZHEIMER%%%'S DISEASE ABNORMAL %%%PHOSPHORYLATION%%% OF THE MICROTUBULE ASSOCIATED PROTEIN %%%TAU%%% IN BIOPSY TISSUE
AUTHOR: POLLOCK N J; MIRRA S S; BINDER L I; WOOD J G
AUTHOR ADDRESS: DEP. ANATOMY, EMORY UNIV. SCH. MED., ATLANTA, GA. 30322.
JOURNAL: 16TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PART 1,
WASHINGTON, D.C., USA, NOV. 9-14, 1986. SOC NEUROSCI ABSTR 12 (1). 1986.
266. %%%1986%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/142 (Item 142 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

05030395 BIOSIS NO.: 000031105527
PP-60C-SRC %%%PHOSPHORYLATES%%% MICROTUBULE-ASSOCIATED PROTEIN 2 AND
%%%TAU%%% ON TYROSINE
AUTHOR: KOSIK K S; NEER E J
AUTHOR ADDRESS: BRIGHAM WOMEN'S HOSP., BOSTON, MASS. 02115.
JOURNAL: 16TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, PART 1,
WASHINGTON, D.C., USA, NOV. 9-14, 1986. SOC NEUROSCI ABSTR 12 (1). 1986.
36. %%%1986%%%
CODEN: ASNEE
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/143 (Item 143 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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05010106 BIOSIS NO.: 000031085238
MICROTUBULE ASSOCIATED PROTEIN %%%TAU%%% IS ABNORMALLY %%%PHOSPHORYLATED%%%
IN %%%ALZHEIMER%%% BRAIN
AUTHOR: GRUNDKE-IQBAL I; IQBAL K; WISNIEWSKI H M
AUTHOR ADDRESS: INST. BASIC RES., STATEN ISLAND, N.Y. 10314.
JOURNAL: 62ND ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF
NEUROPATHOLOGISTS, MINNEAPOLIS, MINN., USA, JUNE 19-22, 1986. J NEUROPATHOL
EXP NEUROL 45 (3). 1986. 379. %%%1986%%%
CODEN: JNENA
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

8/7/144 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02782715 Genuine Article#: MD553 Number of References: 576
Title: ACTIVITY-DEPENDENT DEVELOPMENT OF THE VERTEBRATE NERVOUS-SYSTEM
Author(s): FIELDS RD; NELSON PG
Corporate Source: NICHHD,DEV NEUROBIOL LAB/BETHESDA//MD/20892
Journal: INTERNATIONAL REVIEW OF NEUROBIOLOGY, %%%1992%%%, V34, P133-214
ISSN: 0074-7742
Language: ENGLISH Document Type: REVIEW

8/7/145 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02763581 Genuine Article#: MC395 Number of References: 262
Title: CELLULAR AND MOLECULAR-BIOLOGY OF NEURONAL INTERMEDIATE FILAMENTS
Author(s): FLIEGNER KH; LIEM RKH
Corporate Source: COLUMBIA UNIV COLL PHYS & SURG,DEPT PATHOL/NEW
YORK//NY/10032; COLUMBIA UNIV COLL PHYS & SURG,DEPT ANAT & CELLBIOL/NEW
YORK//NY/10032
Journal: INTERNATIONAL REVIEW OF CYTOLOGY-A SURVEY OF CELL BIOLOGY,
%%%1991%%%, V131, P109-167
ISSN: 0074-7696
Language: ENGLISH Document Type: REVIEW

8/7/146 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02257994 Genuine Article#: KN661 Number of References: 61
Title: CHARACTERIZATION OF ALTERNATIVE ROUTES FOR PROCESSING OF THE
%%%ALZHEIMER%%% BETA-A4-AMYLOID PRECURSOR PROTEIN - DIFFERENTIAL-EFFECTS OF PHORBOL ESTERS AND CHLOROQUINE
Author(s): GANDY SE; CAPORASO GL; RAMABHADRAN TV; SUZUKI T; BUXBAUM JD;
NORDSTEDT C; IVERFELDT K; CZERNIK AJ; NAIRN AC; GREENGARD P
Corporate Source: ROCKEFELLER UNIV,MOLEC & CELLULAR NEUROSCI LAB,1230 YORK
AVE/NEW YORK//NY/10021
Journal: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, %%%1992%%%, V674, DEC
(DEC 31), P203-217
ISSN: 0077-8923
Language: ENGLISH Document Type: ARTICLE

8/7/147 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02257992 Genuine Article#: KN661 Number of References: 52
Title: DEGRADATION OF PROTEINS IN THE MEMBRANE-CYTOSKELETON COMPLEX IN
%%%ALZHEIMERS%%%-DISEASE - MIGHT AMYLOIDOGENIC APP PROCESSING BE JUST
THE TIP OF THE ICEBERG
Author(s): SAITOH T; MASLIAH E; BAUM L; SUNDSMO M; FLANAGAN L; VIKRAMKUMAR
R; KAY MMB
Corporate Source: UNIV CALIF SAN DIEGO,DEPT NEUROSCI,0624/LA JOLLA//CA/92093; UNIV ARIZONA,COLL MED,DEPT MICROBIOL & IMMUNOL/TUCSON//AZ/85724; UNIV ARIZONA,COLL MED,DEPT MED/TUCSON//AZ/85724
Journal: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES,

%%%1992%%%, V674, DEC
(DEC 31), P180-192
ISSN: 0077-8923
Language: ENGLISH Document Type: ARTICLE

8/7/148 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02237388 Genuine Article#: KM295 Number of References: 14
Title: BRAIN LEVELS OF CYTOPLASMIC CASEIN KINASE-2 AND ITS SUBSTRATE
PROTEINS IN %%%ALZHEIMERS%%%-DISEASE
Author(s): AKSENOVA MV; KARASEVA MV; BURBAEVA GS
Corporate Source: RUSSIAN ACAD MED SCI,MENTAL HLTH RES CTR/MOSCOW//RUSSIA/
Journal: BULLETIN OF EXPERIMENTAL BIOLOGY AND MEDICINE, %%%1992%%%, V113,
N6 (JUN), P804-806
ISSN: 0007-4888
Language: ENGLISH Document Type: ARTICLE

8/7/149 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02130742 Genuine Article#: KD144 Number of References: 42
Title: COMPARISON OF METHODS FOR THE INVITRO ASSEMBLY OF POSTMORTEM HUMAN
BRAIN MICROTUBULES THAT RETAIN THE MICROTUBULE-ASSOCIATED PROTEIN
%%%TAU%%%
Author(s): SPARKMAN DR
Corporate Source: UNIV TEXAS,SW MED CTR,DEPT PATHOL,5323 HARRY HINES
BLVD/DALLAS//TX/75235
Journal: JOURNAL OF NEUROSCIENCE METHODS, %%%1992%%%, V45, N1-2 (OCT-NOV)
, P41-53
ISSN: 0165-0270
Language: ENGLISH Document Type: ARTICLE
Abstract: Several methods for the in vitro assembly of microtubules from postmortem human brain were compared for the purpose of obtaining microtubule preparations that best retained their microtubule-associated proteins. The polymerized microtubules from the preparations were examined by negative staining and electron microscopy and shown to consist of well-formed microtubules with varying amounts of abnormal assembly products that differed between methods. The microtubule protein was analyzed by SDS-polyacrylamide gel electrophoresis, quantitative densitometry, as well as trans-blotted onto membranes which were reacted with monoclonal antibodies to tubulin subunits and microtubule-associated proteins. All the preparations were found to contain both the alpha- and beta-tubulin subunits with quantitative differences, but they varied most, both quantitatively and qualitatively, in their content of microtubule-associated proteins. The optimal method for the assembly of soluble tubulin from postmortem human brain cytosol into intact microtubules which specifically retained most of their MAPs, especially %%%tau%%%, employed 4 M glycerol assembly buffer in the presence of 10 muM taxol and 1 mM GTP. The isolation methods were used to compare young and aged brains, and there were fewer microtubule-associated proteins, especially %%%tau%%%,
associated with the microtubules in advanced age, in all preparations.

8/7/150 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

02114823 Genuine Article#: KB767 Number of References: 42
Title: ROLE OF %%%TAU%%% IN THE POLYMERIZATION OF PEPTIDES FROM
BETA-AMYLOID PRECURSOR PROTEIN
Author(s): CAPUTO CB; SYGOWSKI LA; SCOTT CW; SOBEL IRE
Corporate Source: ICI PHARMACEUT GRP,ICI AMER,DEPT PHARMACOL,LW-2/WILMINGTON//DE/19897
Journal: BRAIN RESEARCH, %%%1992%%%, V597, N2 (DEC 4), P227-232
ISSN: 0006-8993
Language: ENGLISH Document Type: ARTICLE
Abstract: The composition of paired helical filaments (PHFs), the intracellular amyloid fibrils that accumulate in the brains of %%%Alzheimer%%% patients, is not completely known. We investigated whether synthetic peptides from beta-amyloid precursor protein (APP) can form PHF-like fibrils. Two peptides formed fibrils morphologically similar to PHFs. The presence of %%%tau%%% protein, a known PHF component, greatly enhanced the numbers of fibrils formed from one peptide, from the C-terminus of APP, and became associated with the fibrils. A %%%tau%%% fragment corresponding to the tubulin-binding region was sufficient to induce fibril formation. %%%Tau%%% did not alter fibril formation by the other peptide, which was from the beta/A4 region of APP. These results raise the possibility that a C-terminal fragment of APP, along with %%%tau%%%, may be involved in PHF formation. Thus the proteolytic processing of APP may generate fragments that contribute to both amyloids and both histopathologic lesions of %%%Alzheimer%%%'s disease.

8/7/151 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02106323 Genuine Article#: KB148 Number of References: 46
Title: CYTOSKELETAL ABNORMALITIES IN %%%ALZHEIMERS%%%-DISEASE
Author(s): LOVESTONE S; ANDERTON B
Corporate Source: INST PSYCHIAT,DEPT NEUROSCI,NEURODEGENERAT DIS GRP,OLD
AGE PSYCHIAT & BRIAN ANDERTON SECT/LONDON SE5 8AF//ENGLAND/
Journal: CURRENT OPINION IN NEUROLOGY AND NEUROSURGERY, %%%1992%%%, V5, N6
(DEC), P883-888
ISSN: 0951-7383
Language: ENGLISH Document Type: ARTICLE
Abstract: A fundamental process in the pathogenesis of %%%Alzheimer%%%'s
disease (AD) is the breakdown of the cytoskeleton. The microscopic manifestation of this - neurofibrillary tangles - is described. Tangles are formed from paired helical filaments (PHF), in turn constructed from abnormally %%%phosphorylated%%% %%%Tau%%% proteins. Recent
investigations on the process of %%%Tau%%% %%%phosphorylation%%% and
possible links between amyloid deposition and tangle formation are reviewed.

8/7/152 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02073599 Genuine Article#: JY566 Number of References: 40
Title: DIFFERENTIAL %%%PHOSPHORYLATION%%% OF %%%TAU%%% BY CYCLIC-AMP
DEPENDENT PROTEIN-KINASE AND CA-2+ CALMODULIN-DEPENDENT PROTEIN
KINASE-II - METABOLIC AND FUNCTIONAL CONSEQUENCES
Author(s): JOHNSON GVW
Corporate Source: UNIV ALABAMA,CTR SPARKS,DEPT PSYCHIAT & BEHAV
NEUROBIOL/BIRMINGHAM//AL/35294
Journal: JOURNAL OF NEUROCHEMISTRY, %%%1992%%%, V59, N6 (DEC), P2056-2062
ISSN: 0022-3042
Language: ENGLISH Document Type: ARTICLE
Abstract: The effects of cyclic AMP-dependent protein kinase (cAMP-PK) or Ca2+/calmodulin-dependent protein kinase II (CaMKII)
%%%phosphorylation%%% on the binding of bovine %%%tau%%% to tubulin and
calpain-mediated degradation of %%%tau%%% were studied. Both

cAMP-PK
and CaMKII readily %%%phosphorylated%%% %%%tau%%% and slowed the
migration of %%%tau%%% on sodium dodecyl sulfate-containing
polyacrylamide gels. However, cAMP-PK %%%phosphorylated%%% %%%tau%%% to
a significantly greater extent than CaMKII (1.5 and 0.9 mol of P-32/mol
of %%%tau%%%, respectively), and %%%phosphorylation%%% of %%%tau%%% by
cAMP-PK resulted in a greater shift to a more acidic, less
heterogeneous pattern on two-dimensional nonequilibrium pH gradient
gels compared with CaMKII %%%phosphorylation%%%. Two-dimensional
phosphopeptide maps indicate that cAMP-PK %%%phosphorylates%%% a site
or sites on %%%tau%%% that are %%%phosphorylated%%% by CaMKII, as well
as a unique site or sites that are not %%%phosphorylated%%% by CaMKII.
%%%Phosphorylation%%% of %%%tau%%% by cAMP-PK significantly decreased
tubulin binding and, as previously reported, also inhibited the
calpain-induced degradation of %%%tau%%%. CaMKII %%%phosphorylation%%%
of %%%tau%%% did not alter either of these parameters. These results
suggest that the %%%phosphorylation%%% of site(s) on the %%%tau%%%
molecule uniquely accessible to cAMP-PK contributed to the decreased
%%%tau%%%-tubulin binding and increased resistance to calpain
hydrolysis.

8/7/153 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02063397 Genuine Article#: JY308 Number of References: 110
Title: PATHOBIOLOGY OF %%%ALZHEIMERS%%%-DISEASE - A MORPHOLOGISTS VIEW
Author(s): SHANKAR SK
Corporate Source: NATL INST MENTAL HLTH & NEUROSCI,DEPT NEUROPATHOL/BANGALORE 560029//INDIA/
Journal: CURRENT SCIENCE, %%%1992%%%, V63, N8 (OCT 25), P430-439
ISSN: 0011-3891
Language: ENGLISH Document Type: REVIEW
Abstract: Perhaps no other disease of the human brain has aroused more interest than %%%Alzheimer%%%'s disease. The subject continues to be a
fertile field for modern neurobiology. The classical morphologic hallmarks include: regional neuronal loss, neurofibrillary tangles (NFT) in neurons and senile plaques (SP) (neuritic plaques) in the neuropil, particularly in limbic and associated cortices. Similar and qualitatively indistinguishable changes occur, though in much smaller numbers, during normal ageing. However, only limited Correlation of these lesions with cognitive dysfunction has been reported. NFT consist of highly insoluble paired helical filaments, considered characteristic of %%%Alzheimer%%%'s disease, and antigenically related straight filaments. These also accumulate within neurites in and around SP. They are derived from cytoskeletal proteins, particularly microtubule associated protein, %%%tau%%%. In contrast, extracellular amyloid filaments, found in the centre of many of the plaques and in meningeal and cortical vessels, appear to be composed of a hydrophobic, low-molecular weight polypeptide, the beta-amyloid protein. It has a novel amino-acid sequence, including a domain thought to be in close association with the plasma cell membrane. Like other amyloids, it is derived from a larger precursor protein and self assembles to form large aggregates. Segments of the beta-amyloid protein, when studied in vitro, have been found to be neurotoxic to mature neurons and neurotrophic to immature ones. Exactly how these aberrant polypeptides in and around the neurons lead to dementia is still a matter of intense investigation. Recent studies have emphasized synaptic loss as a major correlate of cognitive decline. It will, therefore, be important to investigate the role of beta-amyloid in that process.

To explain the evolution and progression of the lesions, a causative role for environmental trace metals has been invoked, but such a role remains unproven. Since it is alleged by some that %%%Alzheimer%%%'s disease is not prevalent in India, cross-cultural epidemiologic studies would be of importance. Its age-specific prevalence and incidence in India, however, remains unknown.

8/7/154 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02007844 Genuine Article#: JU247 Number of References: 40
Title: A SERINE->PROLINE CHANGE IN THE %%%ALZHEIMERS%%% DISEASE-ASSOCIATED
EPITOPE %%%TAU%%%-2 RESULTS IN ALTERED SECONDARY STRUCTURE, BUT
%%%PHOSPHORYLATION%%% OVERCOMES THE CONFORMATIONAL GAP
Author(s): LANG E; OTVOS L
Corporate Source: WISTAR INST,3601 SPRUCE ST/PHILADELPHIA//PA/19104; WISTAR INST,3601 SPRUCE ST/PHILADELPHIA//PA/19104
Journal: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, %%%1992%%%, V188, N1 (OCT 15), P162-169
ISSN: 0006-291X
Language: ENGLISH Document Type: ARTICLE

8/7/155 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01988369 Genuine Article#: JT328 Number of References: 46
Title: MICROTUBULE BUNDLING BY %%%TAU%%% PROTEINS INVIVO - ANALYSIS OF
FUNCTIONAL DOMAINS
Author(s): KANAI Y; CHEN JG; HIROKAWA N
Corporate Source: UNIV TOKYO,SCH MED,DEPT ANAT & CELL BIOL,BUNKYOKU/TOKYO 113//JAPAN/
Journal: EMBO JOURNAL, %%%1992%%%, V11, N11 (NOV), P3953-3961
ISSN: 0261-4189
Language: ENGLISH Document Type: ARTICLE
Abstract: %%%Tau%%% varies both in the N-terminal region (three types) and
in the C-terminal repeated microtubule binding domain (two types), generating six isoforms through alternative splicing. To understand the differences between the isoforms and to determine which domains are important for microtubule bundling, we performed transfection studies on fibroblasts using %%%tau%%% isoforms and deletion mutants to quantify their ability to bundle microtubules. By comparing the isoforms, we found that a longer N-terminal region induced microtubule bundling more efficiently, but changes in the microtubule binding domain did not. Mutants lacking the proline rich region or the repeated domain did not bind to microtubules. Although all the other mutants could bind to and bundle microtubules, deletion in the N-terminal neutral region or the first half of the C-terminal tail caused a significant decrease in microtubule bundling, indicating the importance of these regions in microtubule bundling.

8/7/156 (Item 13 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01964702 Genuine Article#: JP668 Number of References: 74
Title: %%%ALZHEIMER%%% NEUROFIBRILLARY TANGLES CONTAIN 2.1 NM FILAMENTS
STRUCTURALLY IDENTICAL TO THE MICROTUBULE-ASSOCIATED PROTEIN-%%%TAU%%%
- A HIGH-RESOLUTION TRANSMISSION ELECTRON-MICROSCOPE STUDY OF TANGLES
AND SENILE PLAQUE CORE AMYLOID
Author(s): RUBEN GC; IQBAL K; WISNIEWSKI HM; JOHNSON JE; GRUNDKEIQBAL I
Corporate Source: DARTMOUTH COLL,DEPT BIOL SCI/HANOVER//NH/03755; NEW YORK

STATE INST BASIC RES DEV DISABILITIES/STATEN ISL//NY/10314; UNIV CALIF
BERKELEY,DEPT INTEGRAT BIOL/BERKELEY//CA/94720; SRI INT,DEPT
NEUROSCI/MENLO PK//CA/94025
Journal: BRAIN RESEARCH, %%%1992%%%, V590, N1-2 (SEP 11), P164-179
ISSN: 0006-8993
Language: ENGLISH Document Type: ARTICLE
Abstract: %%%Alzheimer%%% neurofibrillary tangles (NFT) and senile plaque
core amyloid (SPCA) isolated from the brain of patients with %%%Alzheimer%%%'s disease were freeze-dried and replicated with a new
platinum-carbon (Pt-C) vertical deposition method for high-resolution transmission electron microscopy (TEM). The resolution of this vertical Pt-C replication method is superior to either of the more conventional 20-degrees rotary replication or 45-degrees unidirectional replication methods and is dependent on the Pt-C film thickness coating the specimen. The paired helical filaments (PHF) observed within the tangles were right-handed helices with a fairly regular twist period averaging 79.3+/-5.9 nm and a fairly regular maximum width averaging 14.9+/-1.0 nm. The PHF regions of minimum width were not regular nd fell into three size categories: 2.4+/-0.3 nm, 4.9+/-0.6 nm and 9.6+/-1.4 nm. In addition to the PHF found in the tangles, a new filament was found within all the tangles. These 2.1+/-0.2 nm diameter filaments were triple-stranded left helices with 1.0+/-0.2 nm diameter strands with a structure identical to bovine %%%tau%%%. Like bovine %%%tau%%% polymer a number of filaments (130 nm to 238 nm) were longer
than a fully stretched %%%tau%%% monomer of 96 nm. Images of neuritic
senile plaque core amyloid (SPCA) showed that amyloid had a more solid appearance than the NFT and its branched filament structures were unlike the approximately 2.1 nm diameter filaments or the PHF found in NFT.

8/7/157 (Item 14 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01955406 Genuine Article#: JP593 Number of References: 48
Title: %%%PHOSPHORYLATION%%% OF %%%TAU%%%-PROTEIN BY PURIFIED P34(CDC28)
AND A RELATED PROTEIN-KINASE FROM NEUROFILAMENTS
Author(s): MAWALDEWAN M; SEN PC; ABDELGHANY M; SHALLOWAY D; RACKER E
Corporate Source: CORNELL UNIV,BIOCHEM & MOLEC & CELL BIOL SECT/ITHACA//NY/14853; CORNELL UNIV,BIOCHEM & MOLEC & CELL BIOL SECT/ITHACA//NY/14853; BOSE INST,DEPT CHEM/CALCUTTA 700009/W
BENGAL/INDIA/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, %%%1992%%%, V267, N27 (SEP 25), P
19705-19709
ISSN: 0021-9258
Language: ENGLISH Document Type: ARTICLE
Abstract: It has been suggested that hyperphosphorylation of the %%%tau%%%
protein in neurofibrillary tangles may be relevant to the etiology of %%%Alzheimer%%%'s disease and that at least one of the hyperphosphorylated sites lies within a consensus sequence for the p34cdc2/cdc28 family of kinases. We describe a new method for large-scale purification of p34cdc28 kinase from Saccharomyces cerevisiae and show that the purified enzyme can %%%phosphorylate%%%
bovine and human %%%tau%%%. %%%Phosphorylation%%% was greatly enhanced
by the addition of basic and acidic substrate modulators. The effect of the substrate modulators differed both with the structures of the substrates and the modulators. Similar results were obtained with a kinase that could be purified from neurofilaments by p13suc1 affinity chromatography, a hallmark of p34cdc2/cdc28-type kinases. These results
are consistent with the hypothesis that a kinase of this type is involved in %%%tau%%% %%%phosphorylation%%% in vivo and open the possibility that hyperphosphorylation in %%%Alzheimer%%%'s disease may
be controlled by substrate modulators.

8/7/158 (Item 15 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01952677 Genuine Article#: JN807 Number of References: 74
Title: APPROPRIATE TARGET INTERACTIONS PREVENT ABNORMAL CYTOSKELETAL
CHANGES IN NEURONS - A STUDY WITH INTRASCIATIC GRAFTS OF THE SEPTUM AND
THE HIPPOCAMPUS
Author(s): DOERING LC
Corporate Source: MCMASTER UNIV,DIV ANAT,HSC 1R1,1200 MAIN ST W/HAMILTON
L8N 3Z5/ONTARIO/CANADA/
Journal: JOURNAL OF NEUROSCIENCE, %%%1992%%%, V12, N9 (SEP), P3399-3413
ISSN: 0270-6474
Language: ENGLISH Document Type: ARTICLE
Abstract: Transplantation of embryonic CNS regions into the PNS provides an
opportunity to study temporal and spatial changes in the cytoskeleton that are associated with aging and neurodegenerative diseases. In this study, the fetal septum was transplanted alone or with the hippocampus into the sciatic nerves of young adult rats to determine whether the proper central neural target could prevent the expression of abnormal cytoskeletal changes. The substantia nigra, a nontarget area of the septum, served as control co-grafts. After 1, 3, 6, 12, and 18 months of survival, the grafts were examined by immunocytochemistry with antibodies to %%%phosphorylated%%% and nonphosphorylated neurofilaments, microtubule-associated proteins (MAPs), and glial fibrillary acidic protein (GFAP).

Subpopulations of neurons in the septal transplants expressed CAT and the NGF receptor (192-IgG). Long-term (12-18 months) expression of these two markers was only observed when the septum was combined with the hippocampus.

Although isolated single grafts of septum survived within the PNS substratum, significant neuronal loss, extensive graft shrinkage, and aberrant cytoskeletal immunoreactivity were prominent in the long-term group. Changes that reflected an aging process included the ectopic expression of %%%phosphorylated%%% neurofilaments in neuronal perikarya, swollen axons, and a loss of MAP2 immunoreactivity that paralleled dendrite regression. In addition, abnormal "curly" fibers in the neuropil were also immunolabeled with an antibody directed against %%%tau%%% (5E2). Introduction of hippocampal co-grafts increased the final size of the septal transplants and prevented the cytoskeletal changes that accompanied the degeneration in the single septal grafts. The degree of GFAP immunostaining in the septum corresponded with advancing graft age and was minimized when grafted with the hippocampal formation. When the septum was combined with the substantia nigra, the grafts also underwent shrinkage and no protective influence from aberrant cytoskeletal staining was observed.

These experiments exemplify the importance of an appropriate CNS neural target on the maintenance of long-term cholinergic neuron survival and normal morphology at the cytoskeletal level and illustrate the usefulness of these CNS-PNS constructs to examine conditions that influence the cytoskeleton.

8/7/159 (Item 16 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01942846 Genuine Article#: JN245 Number of References: 37
Title: NEUROTOXIC EFFECTS OF DIETARY ALUMINUM
Author(s): JOPE RS; JOHNSON GVW
Corporate Source: UNIV ALABAMA,DEPT PSYCHIAT & BEHAV NEUROBIOL/BIRMINGHAM//AL/35294

Journal: CIBA FOUNDATION SYMPOSIA, %%%1992%%%, V169, P254-267
ISSN: 0300-5208
Language: ENGLISH Document Type: ARTICLE
Abstract: Neurochemical responses to chronic oral aluminium administration have been studied in rats. Aluminium (0.3%) was added to drinking water of adult rats for four weeks or longer and weanling rats were given aluminium for eight weeks. Selective cognitive impairment was demonstrated in the adult rats. Aluminium inhibited calcium flux and phosphoinositide metabolism, one product of which (inositol 1,4,5-trisphosphate) modulates intracellular calcium levels. In weanling rats aluminium decreased the in vivo concentration of inositol 1,4,5-trisphosphate in the hippocampus. An increase in cyclic AMP concentrations by 30-70% in various brain regions in adult and weanling rats was found. Aluminium enhanced agonist-stimulated but not basal cyclic AMP production in vitro. It was postulated that aluminium inhibits the GTPase activity of the stimulatory G protein, G(s), leading to prolonged activation of G(s) after receptor stimulation and increased cyclic AMP production. Aluminium treatment also increased the %%%phosphorylation%%% of microtubule-associated protein 2 (MAP-2) and the 200 kDa neurofilament protein (NF-H) but several other phosphoproteins were unaffected. Concentrations of seven structural proteins-MAP-2, %%%tau%%%, NF-H, NF-M (150 kDa), NF-L (68 kDa), tubulin and spectrin-were measured in rat brain regions by immunoblot methods. MAP-2 was most consistently decreased.

These studies show that chronic oral aluminium administration to rats has significant neurochemical consequences. Three sites of action are implicated: altered calcium homeostasis, enhanced cyclic AMP production, and changes in cytoskeletal protein phosplorylation states and concentrations.

8/7/160 (Item 17 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01939271 Genuine Article#: JM812 Number of References: 37
Title: PATHOLOGICAL-CHANGES IN OLFACTORY NEURONS IN %%%ALZHEIMERS%%% -DISEASE
Author(s): TALAMO BR; FENG WH; PEREZCRUET M; ADELMAN L; KOSIK K; LEE VMY; CORK LC; KAUER JS
Corporate Source: TUFTS UNIV,SCH MED,DIV NEUROSCI/BOSTON//MA/02111; NEW ENGLAND MED CTR/BOSTON//MA/02111; HARVARD UNIV,SCH MED/BOSTON//MA/02115 ; UNIV PENN,SCH MED/PHILADELPHIA//PA/19104; JOHNS HOPKINS UNIV,SCH MED/BALTIMORE//MD/21205
Journal: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, %%%1991%%%, V640, DEC (DEC 3), P1-7
ISSN: 0077-8923
Language: ENGLISH Document Type: ARTICLE

8/7/161 (Item 18 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01928586 Genuine Article#: JM262 Number of References: 45
Title: EXPRESSION AND %%%PHOSPHORYLATION%%% OF A 3-REPEAT ISOFORM OF %%%TAU%%% IN TRANSFECTED NONNEURONAL CELLS
Author(s): GALLO JM; HANGER DP; TWIST EC; KOSIK KS; ANDERTON BH
Corporate Source: INST PSYCHIAT,DEPT NEUROSCI,DE CRESPIGNY PK/LONDON SE5 8AF//ENGLAND/; INST PSYCHIAT,DEPT NEUROSCI,DE CRESPIGNY PK/LONDON SE5 8AF//ENGLAND/; KINGS COLL SCH MED & DENT/LONDON//ENGLAND/; BRIGHAM & WOMENS HOSP,CTR NEUROL DIS/BOSTON//MA/02115; INST PSYCHIAT,DEPT NEUROL/LONDON SE5 8AF//ENGLAND/; HARVARD UNIV,SCH MED/BOSTON//MA/02115
Journal: BIOCHEMICAL JOURNAL, %%%1992%%%, V286, SEP (SEP 1), P399-404
ISSN: 0264-6021
Language: ENGLISH Document Type: ARTICLE
Abstract: The neuronal microtubule-associated protein. %%%tau%%%, is expressed as a set of isoforms containing either three or four tandemly repeated 31-amino-acid motifs in the C-terminal half of the molecule that can bind to microtubules. Three-repeat forms are the only ones expressed early in development. A single three-repeat isoform of %%%tau%%% has been stably expressed in non-neuronal cells which do not express endogenous %%%tau%%%. Chinese hamster ovary (CHO) cells were transfected with a full-length cDNA coding for the foetal form of human %%%tau%%% cloned downstream of the simian virus 40 (SV40) promoter, and a cell line constitutively expressing %%%tau%%%, CHO[pSVtau3], was isolated. Double-label immunofluorescence microscopy reveals that %%%tau%%% co-localizes with the microtubular network of normal or taxol-treated CHO[pSVtau3] cells, without inducing any dramatic change in cell morphology. %%%Tau%%% is expressed in CHO[pSVtau3] cells as three bands in SDS/PAGE recognized by antibodies to %%%tau%%%, the slow-migrating %%%tau%%% species being the most abundant. %%%Tau%%% also appears as three bands in a heat-stable fraction from CHO[pSVtau3] cells, but a single band of enhanced immunoreactivity is detected following treatment of this fraction with alkaline phosphatase. This single band co-migrates with the fast-migrating band of untreated fractions or whole-cell extracts. In conclusion, a three-repeat isoform of %%%tau%%% is capable of binding to microtubules in transfected non-neuronal cells; furthermore, in this system, the protein is %%%phosphorylated%%% in at least two different states inducing a reduced electrophoretic mobility.

8/7/162 (Item 19 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01873790 Genuine Article#: JH625 Number of References: 57
Title: IMMUNE ELECTRON-MICROSCOPIC CHARACTERIZATION OF MONOCLONAL-ANTIBODIES TO %%%ALZHEIMER%%% NEUROFIBRILLARY TANGLES
Author(s): WRZOLEK MA; MERZ PA; KASCSAK R; GRUNDKEIQBAL I; IQBAL K; RUBENSTEIN R; TONNADEMASI M; GOLLER NL; MEHTA P; WISNIEWSKI HM
Corporate Source: NEW YORK STATE INST BASIC RES DEV DISABILITIES,1050 FOREST HILL RD/STATEN ISL//NY/10301; NEW YORK STATE INST BASIC RES DEV DISABILITIES,1050 FOREST HILL RD/STATEN ISL//NY/10301
Journal: AMERICAN JOURNAL OF PATHOLOGY, %%%1992%%%, V141, N2 (AUG), P 343-355
Language: ENGLISH Document Type: ARTICLE
Abstract: Characterization of eleven monoclonal antibodies (MAbs), raised to isolated sodium dodecyl sulfate (SDS)-treated %%%Alzheimer%%%'s neurofibrillary tangles (ANT), has revealed the presence of at least two different epitopes. MAbs were tested for reactivity to ubiquitin and paired helical filaments (PHF) isolated by three different procedures. The effect of protease and/or alkaline phosphatase pretreatment on the reactivity of the MAbs with isolated PHF was also examined All MAbs that bad reacted strongly in the ELISA with sonicated SDS-treated ANT also immune decorated isolated PHF to varying degrees.
Two MAbs exhibited a high reactivity to PHF: 3-39 and 5-25. MAb 3-39 was found to recognize a protease sensitive epitope, In contrast MAb 5-25 was found to consistently decorate isolated PHF in all preparations and exhibited a strong reactivity to ubiquitin, and the epitope in isolated PHF was not protease sensitive. Thus structural PHF after protease treatment and detergent treatment contain an antigenic

site that is present in ubiquitin.

8/7/163 (Item 20 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01803684 Genuine Article#: JC177 Number of References: 55
Title: 3-DIMENSIONAL ANALYSIS OF THE RELATIONSHIP BETWEEN SYNAPTIC
PATHOLOGY AND NEUROPIL THREADS IN %%%ALZHEIMER%%%-DISEASE
Author(s): MASLIAH E; ELLISMAN M; CARRAGHER B; MALLORY M; YOUNG S; HANSEN L
; DETERESA R; TERRY RD
Corporate Source: UNIV CALIF SAN DIEGO,DEPT NEUROSCI/LA JOLLA//CA/92093;
UNIV CALIF SAN DIEGO,SAN DIEGO MICROSCOPY & IMAGING RESOURCE/LA
JOLLA//CA/92093
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, %%%1992%%%
, V51, N4 (JUL), P404-414
Language: ENGLISH Document Type: ARTICLE
Abstract: Recent studies have shown that the %%%Alzheimer%%% disease (AD)
neocortex is characterized by a loss of large neurons, the presence of dilated terminal axons, widespread loss of synapses, and a disruption of the dendritic cytoskeleton which is manifested as %%%Tau%%% immunoreactive threads. In the present study we have investigated the relationship between synaptic and dendritic abnormalities in the neocortex of %%%Alzheimer%%% patients and examined the extent to which
these structural alterations correlate with the severity of cognitive impairment in AD. Quantitative neuroanatomical data were obtained from immunofluorescence-labeled specimens using a laser-scanning confocal microscope, computer-assisted image processing and serial section reconstruction techniques. We found that the AD cases showed a 34% loss
in the number of presynaptic terminals per 100 square (sq) mu-m, many of which showed structural abnormalities. The AD neuropil had an average of 10 +/- 7 dendritic threads per 1,000 sq-mu-m, with the average thread measuring 2 sq-mu-m. Severe AD cases had thicker threads
compared with mild to moderate AD cases. Three-dimensional analysis showed clustering of synapses around threads, as well as presynaptic boutons apposed to dendritic neuropil threads. Statistical analysis showed that the strongest correlation was between synapse density and Blessed score of cognitive impairment. Thread counts did not correlate with either but were correlated with tangle counts. Stepwise multiple regression analysis showed that tangle counts, but not threads, strengthened the correlation between Blessed score and synapses. We conclude that synaptic damage may precede dendritic thread and tangle formation, and that threads do not necessarily induce synaptic pathology. Instead, dendrite sprouting in the denervated regions could be associated with increased accumulation of cytoskeletal proteins observed in the dendritic threads.

8/7/164 (Item 21 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01795578 Genuine Article#: JB711 Number of References: 47
Title: EXPRESSION OF %%%TAU%%% PROTEIN IN NONNEURONAL CELLS - MICROTUBULE
BINDING AND STABILIZATION
Author(s): LEE G; ROOK SL
Corporate Source: HARVARD UNIV,SCH MED,PROGRAM NEUROSCI/BOSTON//MA/02115;
BRIGHAM & WOMENS HOSP,CTR NEUROL DIS,DEPT MED,DIV NEUROL/BOSTON//MA/02115
Journal: JOURNAL OF CELL SCIENCE, %%%1992%%%, V102, JUN (JUN), P227-237
Language: ENGLISH Document Type: ARTICLE
Abstract: The microtubule-associated protein %%%tau%%% is a developmentally
regulated family of neuronal phosphoproteins that promotes the assembly and stabilization of microtubules. The carboxy-terminal half of the protein contains three copies of an imperfectly repeated sequence; this region has been found to bind microtubules in vitro. In addition, a fourth copy of the repeat has been found in adult-specific forms of %%%tau%%% protein. To examine the structure and function of %%%tau%%%
protein in vivo, we have transiently expressed fetal and adult forms of %%%tau%%% protein and %%%tau%%% protein fragments in tissue culture
cells. Biochemical analysis reveals full-length products with heterogeneity in post-translational modification synthesized in the cells. Immunofluorescent staining of transfected cells shows that, under our conditions, sequences on both sides of the repeat region are required for in vivo microtubule co-localization. These additional regions may be required either for enhancing microtubule contacts or for proper protein folding in the cell. In our expression system, the bundling of cellular microtubules occurs only in transfections using four-repeat %%%tau%%% constructs; any four-repeat construct capable of
binding is also able to induce bundling. Our data suggest that the presence of bundles is correlated with enhanced microtubule stability; factors that increase stability such as higher levels of %%%tau%%% protein expression or the presence of the fourth repeat, increase the fraction of transfected cells showing bundles. Finally, the presence of %%%tau%%% protein in the cell allows all interphase microtubules to become acetylated, a post-translational modification usually reserved for a subset of stable cellular microtubules.

8/7/165 (Item 22 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01792916 Genuine Article#: JB641 Number of References: 56
Title: SABELUZOLE, A MEMORY-ENHANCING MOLECULE, INCREASES FAST
AXONAL-TRANSPORT IN NEURONAL CELL-CULTURES
Author(s): GEERTS H; NUYDENS R; NUYENS R; CORNELISSEN F; DEBRABANDER M;
PAUWELS P; JANSSEN PAJ; SONG YH; MANDELKOW EM
Corporate Source: JANSSEN RES FDN,DEPT PHYSIOL/B-2340 BEERSE//BELGIUM/; JAN
PALFIJNZIEKENHUIS,DEPT CLIN PHARMACOL/B-2170 MERKSEM//BELGIUM/; JANSSEN
RES FDN,DEPT BIOCHEM PHARMACOL/B-2340 BEERSE//BELGIUM/; MAX PLANCK UNIT
STRUCT MOLEC BIOL/HAMBURG//GERMANY/
Journal: EXPERIMENTAL NEUROLOGY, %%%1992%%%, V117, N1 (JUL), P36-43
Language: ENGLISH Document Type: ARTICLE

8/7/166 (Item 23 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01764430 Genuine Article#: HZ196 Number of References: 45
Title: ABNORMAL EXPRESSION OF ACTIN IN LYMPHOCYTES OF %%%ALZHEIMERS%%%
-DISEASE AND DOWN-SYNDROME PATIENTS
Author(s): JABBOUR W; POUPLARDBARTHELAIX A; HOULGATTE R; EMILE J
Corporate Source: CHU ANGERS,BIOL CELLULAIRE LAB,INSERM,U298/F-49033 ANGERS
01//FRANCE/; CHR ANGERS,INSERM,U298/F-49036 ANGERS//FRANCE/; CHR
ANGERS,SERV NEUROL B/F-49036 ANGERS//FRANCE/
Journal: JOURNAL OF NEUROIMMUNOLOGY, %%%1992%%%, V38, N3 (JUN), P199-208
Language: ENGLISH Document Type: ARTICLE
Abstract: %%%Alzheimer%%%'s disease (AD) is a degenerative disorder of the
central nervous system accompanied by several immunological disturbances and a number of common features exist between AD and

Down's syndrome (DS). High resolution two-dimensional electrophoresis of lymphocyte proteins demonstrates an actin abnormality in AD and DS: a double actin spot instead of the single spot observed in controls. This dual form was studied by pulse-chase experiments and seems to be related to extracellular factors which influence the post-translational modification of actin. These results agree with the immunological disturbances observed in AD and DS, and with the well established hypothesis that AD is a systemic as well as cerebral disease.

8/7/167 (Item 24 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01717048 Genuine Article#: HV352 Number of References: 87
Title: UBIQUITINATION AND ABNORMAL %%%PHOSPHORYLATION%%% OF PAIRED HELICAL FILAMENTS IN %%%ALZHEIMERS%%%-DISEASE
Author(s): IQBAL K; GRUNDKEIQBAL I
Corporate Source: NEW YORK STATE INST BASIC RES DEV DISABILITIES,1050 FOREST HILL RD/STATEN ISL//NY/10314
Journal: MOLECULAR NEUROBIOLOGY, %%%1991%%%, V5, N2-4, P399-410
Language: ENGLISH Document Type: ARTICLE
Abstract: The most characteristic cellular change in %%%Alzheimer%%%'s disease is the accumulation of aberrant filaments, the paired helical filaments (PHF), in the affected neurons. There is growing evidence from a number of laboratories that dementia correlates better with the accumulation of PHF than of the extracellular amyloid, the second major lesion of %%%Alzheimer%%%'s disease. PHF are both morphologically and biochemically unlike any of the normal neurofibrils. The major polypeptides in isolated PHF are microtubule-associated protein %%%tau%%%. %%%Tau%%% in PHF is %%%phosphorylated%%% differently from %%%tau%%% in microtubules. This abnormal %%%phosphorylation%%% of %%%tau%%% in PHF occurs at several sites. The accumulation of abnormally %%%phosphorylated%%% %%%tau%%% in the affected neurons in %%%Alzheimer%%%'s disease brain precedes both the formation and the ubiquitination of the neurofibrillary tangles. In %%%Alzheimer%%%'s disease brain, tubulin is assembly competent, but the in vitro assembly of microtubules is not observed. In vitro, the phosphate groups in PHF are less accessible than those of %%%tau%%% to alkaline phosphatase. The in vitro dephosphorylated PHF polypeptides stimulate microtubule assembly from bovine tubulin. It is hypothesized that a defect in the protein %%%phosphorylation%%%/dephosphorylation system is one of the earliest events in the cytoskeletal pathology in %%%Alzheimer%%%'s disease. Production of nonfunctional %%%tau%%% by its %%%phosphorylation%%% and its polymerization into PHF most probably contributes to a microtubule assembly defect, and consequently, to a compromise in both axoplasmic flow and neuronal function.

8/7/168 (Item 25 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01662628 Genuine Article#: HP989 Number of References: 56
Title: %%%TAU%%%-PROTEIN AND THE ESTABLISHMENT OF AN AXONAL MORPHOLOGY
Author(s): KOSIK KS; CACERES A
Corporate Source: BRIGHAM & WOMENS HOSP,DEPT MED,DIV NEUROL/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT NEUROL/BOSTON//MA/02115
Journal: JOURNAL OF CELL SCIENCE, %%%1991%%%, S15, P69-74
Language: ENGLISH Document Type: ARTICLE
Abstract: Dissociated neuronal cultures from several regions of the nervous system elaborate two populations of neurites which have features of axons and dendrites. The microtubule-associated protein %%%tau%%% appears to segregate to the axon in some of these culture systems, however it does not do so until after the development of morphological polarity. Despite this observation, %%%tau%%% very likely has some role in the development of polarity because in cultured cerebellar macroneurons taken from the rat embryonic day 15 primordial cerebellum, the inhibition of %%%tau%%% expression by antisense techniques resulted in the failure of a single minor neurite to elongate and form an axon-like neurite. %%%Tau%%% antisense given continuously for up to 72 h kept neurons locked in a stage with minor neurites only; however when released from the effects of the antisense they fully recovered. The administration of %%%tau%%% antisense after the development of polarity resulted in the loss of the axon-like neurite, while dendrite-like neurites continued to grow. Together these results suggest that dendritic differentiation in cerebellar macroneurons requires the prior elaboration of an axon-like structure.

8/7/169 (Item 26 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01662626 Genuine Article#: HP989 Number of References: 68
Title: MICROTUBULE PROTEIN-%%%PHOSPHORYLATION%%% IN NEUROBLASTOMA-CELLS AND NEURITE GROWTH
Author(s): DIAZNIDO J; ARMASPORTELA R; CORREAS I; DOMINGUEZ JE; MONTEJO E; AVILA J
Corporate Source: UNIV AUTONOMA MADRID,CSIC,CTR BIOL MOLEC/E-28049 MADRID//SPAIN/
Journal: JOURNAL OF CELL SCIENCE, %%%1991%%%, S15, P51-59
Language: ENGLISH Document Type: ARTICLE
Abstract: The development of highly asymmetrical neurones from undifferentiated neuroblasts involves the extension of processes (axon and dendrites), that depends on the assembly of an inner microtubule scaffolding. Clonal cell lines of neuronal origin, N2A and NIE-115 neuroblastoma cells, have been chosen as model systems to study the modifications of microtubule protein which accompany the outgrowth of axon-like processes (neurites). Neuroblastoma cells grow as proliferating and undifferentiated cells in standard culture medium but can be considered as committed neuronal precursors. Thus, they are characterized by a high content of tubulin, including the minor neuronal-specific beta-3 isoform, and of MAPs including MAP1B and %%%tau%%%-like proteins. Serum withdrawal from the culture medium results in the extension of axon-like processes which is paralleled by a net increase in the amount of assembled tubulin. However, there is not any increase in the total amount of either tubulin or major MAPs which suggests an involvement of other regulatory factors in the promotion of microtubule assembly. Of relevance in this respect is the fact that beta-3-tubulin, MAP1B, and %%%tau%%%-like proteins become %%%phosphorylated%%% during neurite extension.

A casein kinase II-like enzyme may be involved in some of these %%%phosphorylation%%% events. This enzyme is primarily localized to the nuclei in undifferentiated neuroblastoma cells, whereas a wider distribution of the enzyme between the nucleus and the cytoplasm is found in differentiating neuroblastoma cells. It thus appears plausible that a modified sorting of casein kinase II into the nucleus and the cytoplasm may be involved in the triggering of the %%%phosphorylation%%% of microtubule proteins during neuroblastoma cell differentiation.

8/7/170 (Item 27 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01634193 Genuine Article#: HN274 Number of References: 20
Title: DETERGENT-INSOLUBLE CORTICAL LEWY BODY FIBRILS SHARE EPITOPES WITH NEUROFILAMENT AND %%%TAU%%%
Author(s): POLLANEN MS; BERGERON C; WEYER L
Corporate Source: UNIV TORONTO,CTR RES NEURODEGENERAT DIS,TANZ NEUROSCI BLDG,ROOM 121/TORONTO M5S 1A8/ONTARIO/CANADA/; UNIV TORONTO,CTR RES NEURODEGENERAT DIS,TANZ NEUROSCI BLDG,ROOM 121/TORONTO

M5S
1A8/ONTARIO/CANADA/; TORONTO HOSP,TORONTO GEN DIV/TORONTO/ONTARIO/CANADA/
Journal: JOURNAL OF NEUROCHEMISTRY, %%%1992%%%, V58, N5 (MAY), P1953-1956
Language: ENGLISH Document Type: NOTE
Abstract: Lewy bodies are cytoskeletal inclusions associated with neuronal injury and death in idiopathic Parkinson's disease and other neurodegenerative disorders. The chemical composition of the 8-10-nm fibrils of the Lewy body is unknown, although they are related to both normal cytoskeletal elements and paired helical filaments of %%%Alzheimer%%% neurofibrillary tangles. From the Lewy body-rich cerebral cortex of patients with diffuse Lewy body disease we have isolated intact Lewy bodies using a high salt buffer/nonionic detergent gradient centrifugation procedure and extracted the constitutive fibrils with urea and sodium dodecyl sulfate. Urea/detergent-resistant Lewy body fibrils were solubilized with formic acid and found to contain a single protein band of 68 kDa, which was not found in identically prepared normal brain homogenates. The Lewy body derived-polypeptide was recognized on immunoblots by a polyclonal antibody that reacted with both the 68-kDa neurofilament subunit and the microtubule-associated protein %%%tau%%%. The 68-kDa Lewy body protein was not labeled by the monoclonal antibody %%%tau%%%-1 despite prior in vitro enzymatic dephosphorylation. We conclude that the detergent-insoluble component of the cortical Lewy body fibril shares epitopes with neurofilament and %%%tau%%% and may be a posttranslationally modified derivative of either neurofilament or %%%tau%%% with substantially altered biochemical and immunologic properties.

8/7/171 (Item 28 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01633463 Genuine Article#: HN241 Number of References: 22
Title: CHANGE IN THE CYTOSKELETAL SYSTEM IN FIBROBLASTS FROM PATIENTS WITH FAMILIAL %%%ALZHEIMERS%%%-DISEASE
Author(s): TAKEDA M; TATEBAYASHI Y; NISHIMURA T
Corporate Source: OSAKA UNIV,SCH MED,DEPT NEUROPSYCHIAT,1-1-50 FUKUSHIMA,FUKUSHIMA KU/OSAKA 553//JAPAN/
Journal: PROGRESS IN NEURO-PSYCHOPHARMACOLOGY & BIOLOGICAL PSYCHIATRY, %%%1992%%%, V16, N3 (MAY), P317-328
Language: ENGLISH Document Type: REVIEW
Abstract: 1. Fibroblasts were cultured from four patients, two patients from two independent family lines, clinically diagnosed as familial %%%Alzheimer%%%'s disease.

2. Adhesion efficiency to the dish was significantly suppressed with fibroblasts from patients with familial %%%Alzheimer%%%'s disease compared with the cells from the age-matched control.

3. Cytoskeletal systems were visualized by immunofluorescent staining with antibodies against tubulin, actin, and vimentin, showing unique dearrangement of vimentin fibers in fibroblasts from familial %%%Alzheimer%%%'s disease.

4. Regrowth of vimentin fibers after colchicine treatment was slower with fibroblasts from familial %%%Alzheimer%%%'s disease than that of the control.

5. Western blotting analysis showed no change in tubulin, actin, and vimentin, but the size of fodrin in familial %%%Alzheimer%%% fibroblasts were different from that of the control cell.

8/7/172 (Item 29 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01623916 Genuine Article#: HM481 Number of References: 39
Title: MASSIVE ACCUMULATION OF MODIFIED-%%%TAU%%% AND SEVERE DEPLETION OF NORMAL-%%%TAU%%% CHARACTERIZE THE CEREBRAL-CORTEX AND WHITE MATTER OF %%%ALZHEIMERS%%%-DISEASE - DEMONSTRATION USING THE HYDRATED AUTOCLAVING METHOD
Author(s): SHIN RW; IWAKI T; KITAMOTO T; SATO Y; TATEISHI J
Corporate Source: KYUSHU UNIV,FAC MED,INST NEUROL,DEPT NEUROPATHOL/FUKUOKA 812//JAPAN/; NATL HIZEN PSYCHIAT HOSP,NEUROPATHOL LAB/SAGA//JAPAN/; KYUSHU UNIV,FAC MED,INST NEUROL,DEPT NEUROL/FUKUOKA 812//JAPAN/
Journal: AMERICAN JOURNAL OF PATHOLOGY, %%%1992%%%, V140, N4 (APR), P937-945
Language: ENGLISH Document Type: ARTICLE
Abstract: Using the hydrated autoclaving method, a new immunohistochemical procedure to enhance %%%tau%%% immunoreactivity in formalin-fixed brain tissue, the authors recently reported that %%%tau%%% protein is detected in neuronal cell bodies and proximal dendrites, gray matter neuropil, axons, and glial cells in normal human hippocampus and neocortex. In the this study, the authors performed a comparative study of the distribution of normal and modified forms of %%%tau%%% in %%%Alzheimer%%%'s disease (AD) and control brains. In the cerebral cortex and white matter of AD brains, a massive accumulation of modified %%%tau%%% and/or severe depletion of normal %%%tau%%% were documented in all the %%%tau%%% compartments. In mild AD cases, gray matter neuropil, axons, and glial cells were less severely involved than neuronal perikarya. In the controls, neuronal perikarya were often involved by modified %%%tau%%% accumulation, but the other compartments showed normal distribution. These observations suggest that modifications of %%%tau%%% which lead to neurofibrillary lesions in AD may begin in neuronal perikarya and extend to the other %%%tau%%% compartments in advanced stages of the disease.

8/7/173 (Item 30 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01613910 Genuine Article#: HL816 Number of References: 29
Title: A PROTEIN-KINASE ASSOCIATED WITH PAIRED HELICAL FILAMENTS IN %%%ALZHEIMER%%%-DISEASE
Author(s): VINCENT IJ; DAVIES P
Corporate Source: YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT PATHOL/BRONX//NY/10461; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT NEUROSCI/BRONX//NY/10461
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, %%%1992%%%, V89, N7 (APR 1), P2878-2882
Language: ENGLISH Document Type: ARTICLE
Abstract: We have identified a protein kinase in immunoaffinity-purified preparations of paired helical filaments from brain tissue of individuals with %%%Alzheimer%%% disease. The kinase %%%phosphorylates%%% the filament proteins in vitro in a manner independent of second messenger regulation or of modulation by heparin and polyamines. Physiological concentrations of hemin, an oxidized heme porphyrin, inhibit the kinase and abolish Alz-50 immunoreactivity of the proteins. Since paired helical filaments are composed of hyperphosphorylated proteins, association of a protein kinase with the filaments provides a mechanism for abnormal processing of the proteins in disease.

8/7/174 (Item 31 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01570244 Genuine Article#: HJ051 Number of References: 61
Title: %%%TAU%%%-PROTEIN AND NEURODEGENERATION
Author(s): KOSIK KS
Corporate Source: BRIGHAM & WOMENS HOSP,CTR NEUROL DIS,DEPT MED,DIV
NEUROL/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT NEUROL
NEUROSCI/BOSTON//MA/02115
Journal: MOLECULAR NEUROBIOLOGY, %%%1990%%%, V4, N3-4 (FAL-WIN), P171-179
Language: ENGLISH Document Type: ARTICLE
Abstract: Many of the human neurodegenerative conditions involve a reorganization of the neuronal cytoskeleton. The way in which the cytoskeleton is reorganized may provide a clue to the nature of the insult causing the neurodegeneration. The most common of these conditions is %%%Alzheimer%%%'s disease, in which microtubules are lost from neurites that fill up with filamentous structures. One component of the filamentous structures is the microtubule-associated protein (MAP), %%%tau%%%. The %%%tau%%% protein is the product of a single gene expressed predominantly in neurons. The %%%tau%%% gene undergoes complex alternative splicing that is regulated both by development, and by the particular neuronal cell population in which it is expressed. %%%Tau%%% protein can be further modified, following its translation by %%%phosphorylation%%% at several sites. Much of the recent interest in the transition of %%%tau%%% to an abnormal state within a tangle-bearing neuron has focused on %%%phosphorylation%%%. A group of proteins that migrate slightly more slowly than %%%tau%%%, designated PHF-%%%tau%%%, are found in regions of the %%%Alzheimer%%% brain rich in dystrophic neurites, are hyperphosphorylated, fail to bind to microtubules, have distinct solubility properties, and can be derived from fractions of paired helical filaments (PHF).

8/7/175 (Item 32 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01560123 Genuine Article#: HH574 Number of References: 32
Title: CASEIN KINASE-II IS ASSOCIATED WITH NEUROFIBRILLARY TANGLES BUT IS NOT AN INTRINSIC COMPONENT OF PAIRED HELICAL FILAMENTS
Author(s): BAUM L; MASLIAH E; IIMOTO DS; HANSEN LA; HALLIDAY WC; SAITOH T
Corporate Source: UNIV CALIF SAN DIEGO,SCH MED,DEPT NEUROSCI 0624/LA
JOLLA//CA/92093; UNIV CALIF SAN DIEGO,SCH MED,DEPT NEUROSCI 0624/LA
JOLLA//CA/92093; UNIV CALIF SAN DIEGO,SCH MED,CTR MOLEC GENET/LAJOLLA//CA/92093; HLTH SCI CTR,DEPT PATHOL/WINNIPEG R3E
0W1/MANITOBA/CANADA/
Journal: BRAIN RESEARCH, %%%1992%%%, V573, N1 (FEB 21), P126-132
Language: ENGLISH Document Type: ARTICLE
Abstract: Neurofibrillary tangles (NFT) are pathological cytoskeletal structures composed of paired helical filaments (PHF), and are found in neurons of patients afflicted with many neurodegenerative disorders, including %%%Alzheimer%%%'s disease (AD). We previously found that an antiserum against casein kinase II (CK-II) stained NFT intensely in the brain tissue of AD patients. In the current study, we found that the anti-CK-II antiserum stains NFT and neuronal inclusions in many other neurodegenerative diseases as well, including Guam-Parkinson dementia complex, chromosome 18 deletion syndrome, progressive supranuclear palsy, Kufs' disease, and Pick's disease. This antiserum reacted, in crude brain homogenates, with both a doublet of M(r) 43,000 and a M(r) 27,000 Da protein which could correspond to the alpha, alpha', and beta chains of CK-II. The staining of these bands was adsorbed by preincubating anti-CK-II antiserum with purified CK-II. Preincubation of brain sections with purified CK-II strongly intensified the immunostaining of NFT with anti-CK-II, suggesting that NFT may bind CK-II. In the AD brain homogenates, the particulate CK-II levels are increased whereas the cytosolic levels are decreased without a change in total CK-II levels, consistent with the idea that CK-II binds to the particulate PHF, a major constituent of NFT. In accord with these findings, purified PHF bound CK-II, but purified PHF did not contain CK-II as its component. These results suggest that CK-II might be an extraneously deposited component of NFT. Thus, the altered CK-II compartmentalization might have significant consequences in the pathogenesis of AD.

8/7/176 (Item 33 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01558513 Genuine Article#: HH501 Number of References: 37
Title: DIFFERENTIATION OF NEUROBLASTOMA-CELLS CORRELATES WITH AN ALTERED SPLICING PATTERN OF %%%TAU%%%-RNA
Author(s): DEGARCINI EM; CORROCHANO L; WISCHIK CM; NIDO JD; CORREAS I; AVILA J
Corporate Source: UNIV AUTONOMA MADRID,CSIC,CTR BIOL MOLEC/MADRID34//SPAIN/
; MRC,MOLEC BIOL LAB/CAMBRIDGE//ENGLAND/
Journal: FEBS LETTERS, %%%1992%%%, V299, N1 (MAR 2), P10-14
Language: ENGLISH Document Type: ARTICLE
Abstract: Morphological differentiation of N2A neuroblastoma cells is associated with an altered splicing of the gene of the microtubule-associated protein, %%%tau%%%. Two populations of RNA (coding for %%%tau%%% proteins containing three or four tubulin-binding motifs) are present in a similar proportion in undifferentiated neuroblastoma cells while in differentiated cells the proportion is changed in favour of that population coding for %%%tau%%% protein containing four tubulin-binding motifs. An increase in a high molecular weight %%%tau%%% isoforms correlates with the increase in the RNA population coding for four tubulin-binding motifs. A possible consequence of expressing a higher proportion of the %%%tau%%% protein containing four tubulin-binding motifs could be an increase in microtubule stability of differentiated neuroblastoma cells.

8/7/177 (Item 34 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01512952 Genuine Article#: HE275 Number of References: 35
Title: %%%TAU%%%-2 - A PROBE FOR A SER CONFORMATION IN THE AMINO TERMINUS OF %%%TAU%%%
Author(s): WATANABE N; TAKIO K; HASEGAWA M; ARAI T; TITANI K; IHARA Y
Corporate Source: UNIV TOKYO,FAC MED,INST BRAIN RES,DEPT NEUROPATHOL,7-3-1
HONGO,BUNKYO KU/TOKYO 113//JAPAN/; UNIV TOKYO,FAC MED,INST BRAIN
RES,DEPT NEUROPATHOL,7-3-1 HONGO,BUNKYO KU/TOKYO 113//JAPAN/; SCI UNIV
TOKYO,FAC SCI & TECHNOL,DEPT APPL BIOLSCI/NODA/CHIBA 278/JAPAN/;
RIKEN,AGING PROC RES LAB,FRONTIER RES PROGRAM/WAKO//JAPAN/; FUJITA HLTH
UNIV,SCH MED,INST COMPREHENS MED SCI,DIV BIOMED POLYMER SCI/TOYOAKE//JAPAN/; TOKYO METROPOLITAN GERIATR HOSP & INST
GERONTOL,DEPT NEUROPHYSIOL/TOKYO 173//JAPAN/
Journal: JOURNAL OF NEUROCHEMISTRY, %%%1992%%%, V58, N3 (MAR), P960-966
Language: ENGLISH Document Type: ARTICLE
Abstract: We have determined the epitope for %%%Tau%%% 2, a monoclonal antibody that intensely stained tangles, plaque neurites, and curly fibers in the tissue section, and strongly labeled bovine %%%tau%%%, but only very weakly labeled human %%%tau%%% on the blot. The

epitope
has been localized to Ala95 through Ala108 of bovine %%%tau%%%. Ser101
is critical for %%%Tau%%% 2 reactivities; the replacement of Ser by Pro, which is found in rat, mouse, and human %%%tau%%%, brings about very weak %%%Tau%%% 2 reactivities. The strong %%%Tau%%% 2 staining of
tangles and its effective absorption with a synthetic Ser peptide (Ala95 through Ala108) suggest that the %%%tau%%% in paired helical filaments takes a Ser conformation, rather than a Pro conformation, in its amino-terminal portion.

8/7/178 (Item 35 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01507398 Genuine Article#: HE071 Number of References: 37
Title: CASEIN KINASE-II ALTERATION PRECEDES %%%TAU%%%-ACCUMULATION IN
TANGLE FORMATION
Author(s): MASLIAH E; IIMOTO DS; MALLORY M; ALBRIGHT T; HANSEN L; SAITOH T
Corporate Source: UNIV CALIF SAN DIEGO,SCH MED,DEPT NEUROSCI/LA
JOLLA//CA/92093; WHITTIER COLL,DEPT CHEM/WHITTIER//CA/90608
Journal: AMERICAN JOURNAL OF PATHOLOGY, %%%1992%%%, V140, N2 (FEB), P
263-268
Language: ENGLISH Document Type: NOTE
Abstract: Previous studies have shown altered casein kinase II (CK-II) in %%%Alzheimer%%%'s disease (AD). For the present study, the authors analyzed CK-II immunoreactivity at various stages of tangle formation using quantitative laser confocal microscopy and immunoelectron microscopy. AD hippocampal pyramidal cells without neurofibrillary tangles (NFTs) displayed 15% more anti-%%%tau%%% immunoreactivity (P <
0.01) and 43% more anti-CKII immunolabeling than controls (P < 0.001). In AD, tangle-bearing hippocampal neurons with strong anti-%%%tau%%% immunoreactivity (threefold increase from controls) showed a significant 22% increase in anti-CKII immunolabeling (P < 0.01), compared with those without NFTs. Neurons with early neurofibrillary changes showed diffuse anti-CKII immunostaining in their cytoplasm and cell processes. In tangle-bearing neurons, in which a higher level of %%%tau%%% immunoreactivity was detected, anti-CKII immunolabeling was
distributed along a fibrillar meshwork in cell bodies and processes. Linear regression analysis of anti-CKII and anti-%%%tau%%% immunoreactivity in AD showed a positive correlation (r = 0.53, P < 0.001). At the ultrastructural level, anti-CKII was immunolocalized to the paired helical filaments (PHF) of the tangle-bearing neurons, as well as to PHF in neuropil threads and some dystrophic neurites in plaques. These results suggest a possible role for CK-II in tangle formation.

8/7/179 (Item 36 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01494142 Genuine Article#: HD559 Number of References: 52
Title: METAL ION-INDUCED CONFORMATIONAL-CHANGES OF %%%PHOSPHORYLATED%%%
FRAGMENTS OF HUMAN NEUROFILAMENT (NF-M) PROTEIN
Author(s): HOLLOSI M; URGE L; PERCZEL A; KAJTAR J; TEPLAN I; OTVOS L;
FASMAN GD
Corporate Source: BRANDEIS UNIV,DEPT BIOCHEM/WALTHAM//MA/02254; BRANDEIS
UNIV,DEPT BIOCHEM/WALTHAM//MA/02254; L EOTVOS UNIV,INST ORGAN
CHEM/H-1518 BUDAPEST 112//HUNGARY/; SEMMELWEIS UNIV MED SCH,INST
BIOCHEM 1/H-1444 BUDAPEST 8//HUNGARY/; WISTAR INST/PHILADELPHIA//PA/19104
Journal: JOURNAL OF MOLECULAR BIOLOGY, %%%1992%%%, V223, N3 (FEB 5), P
673-682
Language: ENGLISH Document Type: ARTICLE

8/7/180 (Item 37 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

01462355 Genuine Article#: HB185 Number of References: 37
Title: %%%TAU%%%-PROTEINS OF %%%ALZHEIMER%%% PAIRED HELICAL FILAMENTS -
ABNORMAL %%%PHOSPHORYLATION%%% OF ALL 6 BRAIN ISOFORMS
Author(s): GOEDERT M; SPILLANTINI MG; CAIRNS NJ; CROWTHER RA
Corporate Source: MRC,MOLEC BIOL LAB,HILLS RD/CAMBRIDGE CB2 2QH//ENGLAND/;
INST PSYCHIAT,DEPT NEUROPATHOL/LONDON SE5 8AF//ENGLAND/
Journal: NEURON, %%%1992%%%, V8, N1 (JAN), P159-168
Language: ENGLISH Document Type: ARTICLE
Abstract: Preparations of dispersed paired helical filaments(PHFs) from the brains of %%%Alzheimer%%%'s disease and Down's syndrome patients display on gels three principal bands corresponding to abnormally modified forms of the microtubule-associated protein %%%tau%%%. Interpretation of the pattern is difficult because there are six %%%tau%%% isoforms in normal brain and %%%phosphorylation%%% changes
their mobility. By enzymatic dephosphorylation at high temperature, we have shifted the three abnormal bands obtained from dispersed PHFs to align with the six nonphosphorylated %%%tau%%% isoforms. By using antibodies specific for some of the inserts that distinguish the various isoforms and label PHFs, we have established a correspondence between PHFs, abnormal bands, and isoforms. This identification of isoforms is a necessary step in unravelling the molecular pathogenesis of PHFs.

8/7/181 (Item 38 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01456038 Genuine Article#: GZ992 Number of References: 23
Title: DETECTION OF POINT MUTATIONS IN CODON-331 OF MITOCHONDRIAL NADH
DEHYDROGENASE SUBUNIT-2 IN %%%ALZHEIMER%%% BRAINS
Author(s): LIN FH; LIN R; WISNIEWSKI HM; HWANG YW; GRUNDKEIQBAL I;
HEALYLOUIE G; IQBAL K
Corporate Source: NEW YORK STATE INST BASIC RES DEV DISABILITIES/STATEN
ISL//NY/10314
Journal: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, %%%1992%%%, V
182, N1 (JAN 15), P238-246
Language: ENGLISH Document Type: ARTICLE

8/7/182 (Item 39 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01440398 Genuine Article#: GZ100 Number of References: 37
Title: INSITU HYBRIDIZATION OF CALCIUM CALMODULIN DEPENDENT PROTEIN
KINASE-II AND %%%TAU%%%-MESSENGER RNAS - SPECIES-DIFFERENCES AND
RELATIVE PRESERVATION IN %%%ALZHEIMERS%%%-DISEASE
Author(s): MAH VH; ESKIN TA; KAZEE AM; LAPHAM L; HIGGINS GA
Corporate Source: THOMAS JEFFERSON UNIV,DEPT NEUROL,DIV NEUROPATHOL,130 S
9TH ST,SUITE 400/PHILADELPHIA//PA/19107; UNIV ROCHESTER,MED CTR,DEPT
NEUROBIOL & ANAT/ROCHESTER//NY/14642; UNIV ROCHESTER,MED CTR,DEPT

PATHOL/ROCHESTER//NY/14642; NIA,GERONTOL RES CTR,MOLEC NEUROBIOL
SECT/BALTIMORE//MD/21224
Journal: MOLECULAR BRAIN RESEARCH, %%%1992%%%, V12, N1-3 (JAN), P85-94
Language: ENGLISH Document Type: ARTICLE
Abstract: Abnormal %%%phosphorylation%%% of the microtubule associated
protein %%%tau%%% component of neurofibrillary tangles (NFTs) in %%%Alzheimer%%%'s disease (AD) may result from alterations in protein kinase expression. Calcium/calmodulin dependent protein kinase II (CaM kinase II) has been shown to %%%phosphorylate%%% %%%tau%%% in vitro in
such a way to decrease its electrophoretic mobility. A68, apparently a modified form of %%%tau%%% in AD brain, also shows abnormal %%%phosphorylation%%% and slower mobility than %%%tau%%%. To further
examine the role of CaM kinase II in AD, in situ hybridization studies were performed on tissues from rat, monkey and human to examine and compare the patterns of CaM kinase II mRNA expression in different brain regions. The most notable differences among the three species were observed in dendrites in layer I of isocortex, in the molecular layer of the dentate gyrus and stratum radiatum and stratum lacunosum-moleculare in hippocampus, where hybridization was detected in rat, but not in monkey or human brain. In addition, comparisons between %%%tau%%% and CaM kinase II mRNA expression were made in tissue
from normal aged adults and AD patients, especially in areas prone to NFT formation. CaM kinase II and %%%tau%%% mRNAs were co-expressed in
many neuronal populations, both those which are prone to NFT formation as well as those which are rarely affected by AD changes. No major differences in the relative abundance of either CaM kinase II or %%%tau%%% mRNA within particular neuronal populations was noted between
normal aged and AD brain. Diminished hybridization was associated with serve neuronal pathology and cell loss.

8/7/183 (Item 40 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01389961 Genuine Article#: GV176 Number of References: 84
Title: THE %%%ALZHEIMER%%% AMYLOID PRECURSOR IS ASSOCIATED WITH THE
DETERGENT-INSOLUBLE CYTOSKELETON
Author(s): REFOLO LM; WITTENBERG IS; FRIEDRICH VL; ROBAKIS NK
Corporate Source: CUNY MT SINAI SCH MED,DEPT PSYCHIAT,BOX 1229,1 GUSTAVE
LEVY PL/NEW YORK//NY/10029; CUNY MT SINAI SCH MED,DEPT PSYCHIAT,BOX
1229,1 GUSTAVE LEVY PL/NEW YORK//NY/10029; CUNY MT SINAI SCH
MED,FISHBERG RES CTR NEUROBIOL/NEW YORK//NY/10029; CUNY MT SINAI SCH
MED,BROOKDALE CTR MOLEC BIOL/NEW YORK//NY/10029
Journal: JOURNAL OF NEUROSCIENCE, %%%1991%%%, V11, N12, P3888-3897
Language: ENGLISH Document Type: ARTICLE
Abstract: The amyloid beta-protein (A-beta-P), the main component of neuritic plaques in %%%Alzheimer%%%'s disease (AD), is derived by unknown mechanisms from a family of amyloid precursor proteins (APPs). Using a detergent extraction procedure, we have found that in brain and in neural cell lines, 50-90% of APP is bound to detergent-insoluble cytoskeleton. Labeling experiments performed in a C6 glioma cell line indicated that both cell surface and intracellular APPs are associated with the cytoskeleton. This association requires intact microtubules and is modulated by protein %%%phosphorylation%%% and by cell density. These findings suggest that the function of cellular APP, presently unknown, involves the cytoskeleton and particularly microtubules. The dynamic nature of the binding and its dependence on microtubules and protein %%%phosphorylation%%% suggest it as a possible target in AD, where abnormal cytoskeletal structures and protein %%%phosphorylation%%% have been reported. Altered cytoskeletal binding
of APP might lead to its aberrant proteolysis and generation of the A-beta-P.

8/7/184 (Item 41 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01328381 Genuine Article#: GP804 Number of References: 63
Title: THE MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% FORMS A TRIPLE-STRANDED
LEFT-HAND HELICAL POLYMER
Author(s): RUBEN GC; IQBAL K; GRUNDKEIQBAL I; WISNIEWSKI HM; CIARDELLI TL;
JOHNSON JE
Corporate Source: DARTMOUTH COLL,DEPT BIOL SCI/HANOVER//NH/03755; NEW YORK
STATE INST BASIC RES DEV DISABILITIES/STATEN ISL//NY/10314; DARTMOUTH
COLL,HITCHCOCK MED CTR,DARTMOUTH MED SCH,DEPT PHARMACOL/HANOVER//NH/03756; UNIV CALIF BERKELEY,DEPT INTEGRAT
BIOL/BERKELEY//CA/94720; SRI INT,DEPT NEUROSCI/MENLO PK//CA/94025
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, %%%1991%%%, V266, N32, P
22019-22027
Language: ENGLISH Document Type: ARTICLE
Abstract: High resolution transmission electron microscopy (TEM) has shown that bovine %%%tau%%% are 2.1 +/- 0.2-nm diameter filaments which are triple-stranded left-hand helical structures composed of three 1.0 +/- 0.2-nm strands. The reported amino acid sequence of human and bovine %%%tau%%% have been computer processed to predict secondary structure.
Within the constraints imposed by the images, the secondary structure models and other structural information have been used to calculate %%%tau%%%'s maximum and minimum length. The length calculations and secondary structure form the basis for image interpretation. This work indicates that each approximately 1.0-nm strand is a %%%tau%%% polypeptide chain and that the approximately 2.1-nm filament is composed of three separate %%%tau%%% chains (%%%tau%%%-3). Bovine
%%%tau%%% length measurements indicate that %%%tau%%% trimer filaments
are generally longer than a fully extended %%%tau%%% monomer. These measurements indicate that each trimer, %%%tau%%%-3, is joined with other trimers to form long %%%tau%%% polymers, (tau3)n. An inverse temperature transition has been found in the circular dichroism spectrum of %%%tau%%% indicating that its structure is less ordered below 20-degrees-C and more ordered at 37-degrees-C. The implications of this phenomenon with respect to %%%tau%%%'s temperature-dependent
ability to reconstitute microtubules is discussed and a mechanism for the possible abnormal aggregation of %%%tau%%% into neurofibrillary tangles in %%%Alzheimers%%% disease is proposed.

8/7/185 (Item 42 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01299374 Genuine Article#: GM780 Number of References: 68
Title: %%%TAU%%%-PROTEIN BINDS TO MICROTUBULES THROUGH A FLEXIBLE ARRAY OF
DISTRIBUTED WEAK SITES
Author(s): BUTNER KA; KIRSCHNER MW
Corporate Source: UNIV CALIF SAN FRANCISCO,DEPT BIOCHEM/SAN FRANCISCO//CA/94143
Journal: JOURNAL OF CELL BIOLOGY, %%%1991%%%, V115, N3, P717-730
Language: ENGLISH Document Type: ARTICLE
Abstract: %%%Tau%%% protein plays a role in the extension and maintenance
of neuronal processes through a direct association with microtubules. To characterize the nature of this association, we have synthesized a collection of %%%tau%%% protein fragments and studied their binding properties. The relatively weak affinity of %%%tau%%% protein for

microtubules (approximately 10(-7) M) is concentrated in a large region containing three or four 18 amino acid repeated binding elements. These are separated by apparently flexible but less conserved linker sequences of 13-14 amino acids that do not bind. Within the repeats, the binding energy for microtubules is delocalized and derives from a series of weak interactions contributed by small groups of amino acids. These unusual characteristics suggest %%%tau%%% protein can assume multiple conformations and can pivot and perhaps migrate on the surface of the microtubule. The flexible structure of the %%%tau%%% protein binding interaction may allow it to be easily displaced from the microtubule lattice and may have important consequences for its function.

8/7/186 (Item 43 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01286419 Genuine Article#: GL457 Number of References: 20
Title: CYTOSKELETON PATHOLOGY IN %%%ALZHEIMERS%%%-DISEASE AND RELATED DISORDERS
Author(s): SEITELBERGER F; LASSMANN H; BANCHER C
Corporate Source: AUSTRIAN ACAD SCI,INST HIRNFORSCH/A-1090 VIENNA//AUSTRIA/ ; UNIV VIENNA,INST NEUROL/A-1090 VIENNA//AUSTRIA/
Journal: JOURNAL OF NEURAL TRANSMISSION-GENERAL SECTION, %%%1991%%%, S33, P 27-33
Language: ENGLISH Document Type: ARTICLE
Abstract: The reported findings suggest that ubiquitination of pathological proteinaceous intracytoplasmic inclusions is not at all specific of AD. On the contrary it appears to be a general biochemical marker for disorders in the degradation of a variety of cytoskeletal and other cytoplasmic proteins. The pattern of affected cytoskeletal components is not specific of AD/SDAT tangles. %%%Tau%%% definitely is present also in PSP tangles and possibly in Pick bodies but not in Lewy bodies.

Therefore it has to be considered that the intracytoplasmic accumulation of cytoskeletal protein/ubiquitin complexes in itself is a rather unspecific cellular reaction pattern, possibly a secondary reaction to cell injury of many types, especially, however, of neuronal aging. Nevertheless, the manifestation of NFT in an excessive quantity, intensity, and dynamics with severe concomitant lesions as in AD/SDAT undoubtedly is a true pathological and in this sense a disease-specific change.

8/7/187 (Item 44 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01270465 Genuine Article#: GK144 Number of References: 28
Title: SKEIN-LIKE INCLUSIONS IN THE ANTERIOR HORN CELLS IN MOTOR-NEURON DISEASE
Author(s): MIZUSAWA H; NAKAMURA H; WAKAYAMA I; YEN SHC; HIRANO A
Corporate Source: UNIV TSUKUBA,INST CLIN MED,DEPT NEUROL/TSUKUBA 305//JAPAN/; WAKAYAMA MED COLL,DIV NEUROL DIS/WAKAYAMA//JAPAN/; TOTTORI UNIV,DEPT NEUROPATHOL/TOTTORI 680//JAPAN/; YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT PATHOL NEUROPATHOL/BRONX//NY/10461; MONTEFIORE MED CTR,DEPT PATHOL NEUROPATHOL/BRONX//NY/10467
Journal: JOURNAL OF THE NEUROLOGICAL SCIENCES, %%%1991%%%, V105, N1, P14-21
Language: ENGLISH Document Type: ARTICLE
Abstract: Skein-like inclusions (SLIs) in the anterior horn cells of patients with motor neuron diseases, including familial amyotrophic lateral sclerosis with posterior column degeneration, sporadic lower motor neuron disease and classical amyotrophic lateral sclerosis, were investigated morphologically with hematoxylin and eosin preparations, immunostaining for ubiquitin and immunoelectron microscopy. The SLIs were thready linear or tubular structures which immunostained with antiubiquitin antibodies. They were detected on hematoxylin and eosin preparations as eosinophilic thread-like structures often surrounded by pale areas. SLIs were occasionally present as networks of threads or tubules. Sometimes, they were aggregated and formed larger pale inclusions. Ultrastructurally, the SLIs were bundles of filaments which appeared thicker than neurofilaments. The SLIs tended to have central hollow spaces which were devoid of filaments. When the SLIs were clustered, fuzzy thick filaments were randomly and loosely arranged among the individual SLIs. The SLIs were histologically and ultrastructurally distinct from other inclusions such as Bunina bodies and hyaline inclusions. This unique morphology of SLIs may provide a novel perspective on the degenerative processes of the anterior horn cells in MND.

8/7/188 (Item 45 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01256998 Genuine Article#: GH896 Number of References: 47
Title: ABERRANT LOCALIZATION OF MAP5 IMMUNOREACTIVITY IN THE HIPPOCAMPAL-FORMATION IN %%%ALZHEIMERS%%%-DISEASE
Author(s): GEDDES JW; LUNDGREN K; KIM YK
Corporate Source: UNIV KENTUCKY,SANDERS BROWN CTR AGING,209 SANDERS BROWN BLDG/LEXINGTON//KY/40536; UNIV KENTUCKY,DEPT ANAT & NEUROBIOL/LEXINGTON//KY/40536; UNIV CALIF IRVINE,DIV NEUROSURG/IRVINE//CA/92717
Journal: JOURNAL OF NEUROSCIENCE RESEARCH, %%%1991%%%, V30, N1, P183-191
Language: ENGLISH Document Type: ARTICLE
Abstract: Immunocytochemistry was used to examine MAP5 immunoreactivity in the hippocampal formation obtained postmortem from five elderly, normal individuals, six individuals with %%%Alzheimer%%%'s disease (AD), and two "transition" cases that did not have a history of dementia but did exhibit significant AD pathology. In all of the cases examined, axonal staining was restricted to the mossy fibers and their terminal field in CA3 stratum lucidum. In control cases, MAP5 immunoreactivity was observed in the neuronal cytoplasm and the proximal portion of the apical dendrites of pyramidal and granule cells. In both AD and transition cases, increased intensity of immunostaining was observed in CA3 pyramidal, subicular, and dentate gyrus granule cell neurons. Within individual neurons, immunoreactivity filled the neuronal perikarya, including the nuclear region, and the apical dendrite. Punctate staining was observed in neuritic plaques, but neurofibrillary tangles and neuropil threads were not immunostained.

The increase and altered distribution of MAP5 immunoreactivity in both vulnerable and nonvulnerable neurons in AD may reflect an aberrant sprouting response. The increased expression of early cytoskeletal proteins may be tolerated in some regions such as CA3, but not in others including CA1 where the increased expression appear to precede aberrant %%%phosphorylation%%%, proteolysis, and incorporation of cytoskeletal proteins into AD pathology. Alternatively, the results could reflect sprouting in response to the neuronal loss and degeneration.

8/7/189 (Item 46 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01245899 Genuine Article#: GH295 Number of References: 27
Title: MICROTUBULE DESTABILIZATION BY CDC2/H1 HISTONE KINASE - %%%PHOSPHORYLATION%%% OF A PRO-RICH REGION IN THE MICROTUBULE-BINDING DOMAIN OF MAP-4
Author(s): AIZAWA H; KAMIJO M; OHBA Y; MORI A; OKUHARA K; KAWASAKI H; MUROFUSHI H; SUZUKI K; YASUDA H
Corporate Source: UNIV TOKYO,DIV SCI,DEPT BIOPHYS & BIOCHEM/TOKYO113//JAPAN/; UNIV TOKYO,DIV SCI,DEPT BIOPHYS

&
BIOCHEM/TOKYO113//JAPAN/; TOKYO METROPOLITAN INST MED SCI,DEPT MOLEC
BIOL/TOKYO 113//JAPAN/; KANAZAWA UNIV,FAC PHARMACEUT SCI,DEPT
BIOL/KANAZAWA/ISHIKAWA 920/JAPAN/
Journal: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, %%%1991%%%, V
179, N3, P1620-1626
Language: ENGLISH Document Type: ARTICLE

8/7/190 (Item 47 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01231736 Genuine Article#: GG430 Number of References: 50
Title: CHARACTERIZATION OF MAIZE MICROTUBULE-ASSOCIATED PROTEINS, ONE OF
WHICH IS IMMUNOLOGICALLY RELATED TO %%%TAU%%%
Author(s): VANTARD M; SCHELLENBAUM P; FELLOUS A; LAMBERT AM
Corporate Source: UNIV STRASBOURG 1,INST BIOL MOLEC PLANTES,CNRS,12 RUE GEN
ZIMMER/F-67084 STRASBOURG//FRANCE/; HOP KREMLIN
BICETRE,INSERM,U96/F-94275 LE KREMLIN BICETR//FRANCE/
Journal: BIOCHEMISTRY, %%%1991%%%, V30, N38, P9334-9340
Language: ENGLISH Document Type: ARTICLE
Abstract: Microtubule-associated proteins (MAPs) are identified as proteins that copurify with tubulin, promote tubulin assembly, and bind to microtubules in vitro. Higher plant MAPs remain mostly unknown. One example of non-tubulin carrot proteins, which bind to neural microtubules and induce bundling, has been reported so far [Cyr, R. J., & Palewitz, B. A. (1989) Planta 177, 245-260]. Using taxol, we developed an assay where higher plant microtubules were induced to self-assemble in cytosolic extracts of maize cultured cells and were used as the native matrix to isolate putative plants MAPs. Several polypeptides with an apparent molecular masses between 170 and 32 kDa copolymerized with maize microtubules. These putative maize MAPs also coassembled with pig brain tubulin through two cycles of temperature-dependent assembly-disassembly. They were able to initiate and promote MAP-free tubulin assembly under conditions of nonefficient self-assembly and induced bundling of both plant and neural microtubules. One of these proteins, of about 83 kDa, cross-reacted with affinity-purified antibodies against rat brain %%%tau%%% proteins, suggesting the presence of common epitope(s) between neural %%%tau%%%
and maize proteins. This homology might concern the tubulin-binding domain, as plant and neural tubulins are highly conserved and the plant polypeptides coassembled with brain tubulin.

8/7/191 (Item 48 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

01229489 Genuine Article#: GG030 Number of References: 42
Title: HIGH-MOLECULAR-WEIGHT %%%TAU%%% - PREFERENTIAL LOCALIZATION IN THE
PERIPHERAL NERVOUS-SYSTEM
Author(s): GEORGIEFF IS; LIEM RKH; MELLADO W; NUNEZ J; SHELANSKI ML
Corporate Source: COLUMBIA UNIV,ALZHEIMERS DIS RES CTR,DEPT PATHOL,630 W
168TH ST/NEW YORK//NY/10032; COLUMBIA UNIV,ALZHEIMERS DIS RES CTR,DEPT
PATHOL,630 W 168TH ST/NEW YORK//NY/10032; COLUMBIA UNIV,ALZHEIMERS DIS
RES CTR,DEPT PATHOL,630 W 168TH ST/NEW YORK//NY/10032; COLUMBIA UNIV
COLL PHYS & SURG,CTR NEUROBIOL & BEHAV/NEW YORK//NY/10032; HOP HENRI
MONDOR,INSERM,U282/F-94010 CRETEIL//FRANCE/
Journal: JOURNAL OF CELL SCIENCE, %%%1991%%%, V100, SEP, P55-60
Language: ENGLISH Document Type: ARTICLE
Abstract: Using epitope mapping we have demonstrated that a high molecular
weight protein (M(r) approximately 115x10(3)) present in brain and spinal cord is a member of the %%%tau%%% family of microtubule-associated proteins. Antibodies directed against the amino-terminal, middle and carboxyl-terminal portions of %%%tau%%% recognize this protein. A limited survey of neuronal tissues has shown that this high molecular weight %%%tau%%% protein is present in brain, spinal cord, dorsal root ganglia, dorsal and ventral roots and peripheral nerves. High molecular weight %%%tau%%% protein is expressed at higher levels in spinal cord than in brain and is the only form of %%%tau%%% detected in the adult peripheral nervous system.

8/7/192 (Item 49 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

01228550 Genuine Article#: GG037 Number of References: 4
Title: STRUCTURE, ELASTICITY AND %%%PHOSPHORYLATION%%% OF
MICROTUBULE-ASSOCIATED PROTEIN-%%%TAU%%%
Author(s): STEINER B; MANDELKOW EM; LICHTENBERG B; BIERNAT J; GUSTKE N;
MANDELKOW E
Corporate Source: DESY,MAX PLANCK UNIT STRUCT MOLEC BIOL/D-2000 HAMBURG
52//FED REP GER/
Journal: JOURNAL OF MUSCLE RESEARCH AND CELL MOTILITY, %%%1991%%%, V12, N5
, P496
Language: ENGLISH Document Type: MEETING ABSTRACT

8/7/193 (Item 50 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01212160 Genuine Article#: GE895 Number of References: 46
Title: DEMONSTRATION OF A NOVEL NEUROFILAMENT ASSOCIATED ANTIGEN WITH THE
NEUROFIBRILLARY PATHOLOGY OF %%%ALZHEIMER%%% AND RELATED DISEASES
Author(s): GHEUENS J; CRAS P; PERRY G; BOONS J; CEUTERICKDEGROOTE C; LUBKE
U; MERCKEN M; TABATON M; GAMBETTI PL; VANDERMEEREN M; MULVIHILL P;
SIEDLAK S; VANHEUVERSWIJN H; MARTIN JJ
Corporate Source: UNIV INSTELLING ANTWERP,BORN BUNGE FDN,NEUROBIOL
LAB/B-2610 WILRIJK//BELGIUM/; UNIV INSTELLING ANTWERP,NEUROPATHOL
LABS/B-2610WILRIJK//BELGIUM/; CASE WESTERN RESERVE UNIV,INST PATHOL,DIV
NEUROPATHOL/CLEVELAND//OH/44106; INNOGENET/GHENT//BELGIUM/
Journal: BRAIN RESEARCH, %%%1991%%%, V558, N1, P43-52
Language: ENGLISH Document Type: ARTICLE
Abstract: A monoclonal antibody, termed NFT200, was raised after in vitro immunization with sonicated neurofibrillary tangle (NFT)-enriched fractions prepared from %%%Alzheimer%%% brain. The antigen to which NFT200 is directed was expressed in the paired helical filaments of NFT in sporadic and familial %%%Alzheimer%%% disease (AD), in the straight filaments of NFT in AD, progressive supranuclear palsy and of Pick bodies, and the NFT in several other conditions such as Parkinson-dementia complex of Guam and subacute sclerosing panencephalitis. Granulovacuolar degeneration of AD was also labeled with NFT200. Hirano bodies and amyloid deposits in AD, as well as Lewy bodies of idiopathic Parkinson disease lacked in the antigen. The NFT200-antigen was also expressed as a phosphatase-insensitive antigen in normal neurofilaments found in spinal cord and peripheral nerve axons but was absent from the perikaryal accumulation of neurofilaments induced by aluminum intoxication. Nevertheless, immunoblot studies failed to detect the NFT200 in isolated preparations of the neurofilament proteins, MAP-2, %%%tau%%%, ubiquitin or A4-amyloid peptide. The results indicate that the NFT200 monoclonal antibody is directed against a phosphatase-insensitive epitope of an axonal protein associated with neurofilaments but is labile to isolation and expressed as a stable epitope of a 200 kDa component of NFT.

8/7/194 (Item 51 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01199639 Genuine Article#: GD742 Number of References: 34
Title: EFFECTS OF ALUMINUM ON %%%TAU%%%-PROTEINS IN HUMAN
NEUROBLASTOMA-CELLS
Author(s): MESCO ER; KACHEN C; TIMIRAS PS
Corporate Source: NIA,FRANCIS SCOTT KEY MED CTR,GERONTOL RES CTR,4940
EASTERN AVE/BALTIMORE//MD/21224; UNIV CALIF BERKELEY,DEPT MOLEC &
CELLULAR BIOL/BERKELEY//CA/94720
Journal: MOLECULAR AND CHEMICAL NEUROPATHOLOGY, %%%1991%%%, V14, N3, P
199-212
Language: ENGLISH Document Type: ARTICLE
Abstract: The presence of the trivalent metallic cations, aluminum and boron, in the culture medium of differentiated human LAN-5 neuroblastoma cells results in increased amounts of specific isomers of microtubule-associated %%%tau%%% proteins. The cells were differentiated to a neuronal phenotype by the addition of retinoic acid. Six-day exposures of the differentiated cells to a 1-mM dose of aluminum or boron yielded increases in %%%tau%%% protein immunoreactivity to the monoclonal antibodies %%%Tau%%%-1 and Alz-50.
Significant increases in immunoreactivity were seen at treatment levels of aluminium down to 100-mu-M. The increases in %%%tau%%% proteins were independent from increases in levels of total cell protein. Control cultures treated with the divalent cations zinc and iron showed no increases in levels of %%%tau%%% proteins.

8/7/195 (Item 52 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01195142 Genuine Article#: GD197 Number of References: 25
Title: 2 TYPES OF SPHEROID BODIES IN THE NIGRAL NEURONS IN PARKINSONS-DISEASE
Author(s): YAMADA T; AKIYAMA H; MCGEER PL
Corporate Source: UNIV BRITISH COLUMBIA,DEPT PSYCHIAT,KINSMEN LABNEUROL
RES,2255 WESBROOK MALL/VANCOUVER V6T 1W5/BC/CANADA/; UNIV BRITISH
COLUMBIA,CTR NEURODEGENERAT DIS/VANCOUVER V6T 1W5/BC/CANADA/
Journal: CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES, %%%1991%%%, V18, N3, P
287-294
Language: ENGLISH Document Type: ARTICLE
Abstract: Dendritic spheroid bodies (SBs) and Lewy bodies (LBs) were identified in comparable numbers in the substantia nigra pars compacta (SBC) of nine parkinsonian cases and one case of striatonigral degeneration but were not found in cases of Huntington's disease or neurologically normal controls. The immunohistochemical profile of the SBs in dystrophic dendrites of nigrostriatal dopaminergic neurons was remarkably similar to that of the LBs found within dendrites or free of the SNC neuropil. Both types of inclusions stained positively with antibodies to tyrosine hydroxylase, ubiquitin and microtubule-associated protein-2 (MAP2), and negatively for %%%Tau%%%
-2, although they had different ultrastructural appearances. A few intracellular LBs were stained by antibodies to neurofilament proteins (NFs) 68, 160, and 200 kD, but dendritic SBs and extracellular LBs were not so stained. These data indicate that dendritic SBs and extracellular LBs may have a common molecular pathogenetic origin in Parkinson's disease. On the other hand, the SBs seen in the pars reticulata (SNR) and in the distal nigrostriatal axons even in control cases were generally stained by antibodies to NFs and ubiquitin but not to MAP2. This latter staining pattern in similar to that shown by SBs in the anterior horn in ALS and in the cerebellum of neurologically normal brains and is believed typical of axonal as opposed to dendritic SBs.

8/7/196 (Item 53 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01117971 Genuine Article#: FX450 Number of References: 22
Title: INCREASED CYTOSOLIC FREE CALCIUM IN LYMPHOCYTES OF %%%ALZHEIMER%%%
PATIENTS
Author(s): ADUNSKY A; BARAM D; HERSHKOWITZ M; MEKORI YA
Corporate Source: MEIR HOSP,ALLERGY IMMUNOL UNIT/IL-44281 KEFAR
SAVA//ISRAEL/; MEIR HOSP,ALLERGY IMMUNOL UNIT/IL-44281 KEFAR
SAVA//ISRAEL/; CHAIM SHEBA MED CTR,DEPT GERIATR MED/TEL AVIV//ISRAEL/;
CHAIM SHEBA MED CTR,DEMENTIA CLIN/TEL AVIV//ISRAEL/; TEL AVIV
UNIV,SACKLER SCH MED/TEL AVIV//ISRAEL/
Journal: JOURNAL OF NEUROIMMUNOLOGY, %%%1991%%%, V33, N2, P167-172
Language: ENGLISH Document Type: ARTICLE
Abstract: Free cytosolic calcium content [Ca2+]i was determined in peripheral blood mononuclear cells (PBMC) from healthy volunteers, %%%Alzheimer%%%'s disease and multi-infarct dementia patients. Measurement of [Ca2+]i by the fluorescent dye quin-2, before and at several time intervals during incubation with phytohemagglutinin (PHA), showed a higher resting [Ca2+]i in PBMC of %%%Alzheimer%%%'s disease patients as compared to controls and multi-infarct dementia patients. However, the addition of supra-optimal PHA doses (100-mu-g/ml) induced strikingly higher [Ca2+]i levels in %%%Alzheimer%%%'s disease patients (1647 +/- 200 nM versus 398 +/- 27 nM in controls, and 346 +/- 40 nM in multi-infarct dementia patients). The increased [Ca2+]i concentration was also found after a specific stimulation with a monoclonal anti-CD3 antibody. The results may have important implications in understanding the pathophysiology of %%%Alzheimer%%%'s disease and suggest that [Ca2+]i may prove diagnostically valuable.

8/7/197 (Item 54 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01106841 Genuine Article#: FW806 Number of References: 50
Title: A PROGRESSIVE DEPOSITION OF PAIRED HELICAL FILAMENTS (PHF) IN THE
BRAIN CHARACTERIZES THE EVOLUTION OF DEMENTIA IN %%%ALZHEIMERS%%%
-DISEASE - AN IMMUNOCYTOCHEMICAL STUDY WITH A MONOCLONAL-ANTIBODY
AGAINST THE PHF CORE
Author(s): MENA R; WISCHIK CM; NOVAK M; MILSTEIN C; CUELLO AC
Corporate Source: MCGILL UNIV,DEPT PHARMACOL & THERAPEUT,MCINTYREMED SCI
BLDG,3655 DRUMMOND ST/MONTREAL H3G 1Y6/QUEBEC/CANADA/; MCGILL UNIV,DEPT
PHARMACOL & THERAPEUT,MCINTYREMED SCI BLDG,3655 DRUMMOND ST/MONTREAL
H3G 1Y6/QUEBEC/CANADA/; UNIV CAMBRIDGE,ADDENBROOKES HOSP,DEPT
PSYCHIAT/CAMBRIDGE CB2 2QQ//ENGLAND/; SLOVAK ACAD SCI/CS-80936
BRATISLAVA//CZECHOSLOVAKIA/; MRC,MOLEC BIOL LAB/CAMBRIDGE//ENGLAND/
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, %%%1991%%%
, V50, N4, P474-490
Language: ENGLISH Document Type: ARTICLE
Abstract: Using the monoclonal antibody (mAb) 6.423 which recognizes epitopes of the pronase-resistant core of paired helical filaments (PHF), we studied postmortem frontal cortex from %%%Alzheimer%%%'s disease (AD) patients with short (Group II) and long (Group III) histories of clinical dementia. Four cases with clinically unconfirmed dementia and a postmortem diagnosis of AD (Group I) were also studied. In Group I, the 6.423 mAb was negative whereas in Group II, the antibody recognized primarily neurofibrillary tangles (NFT). In

contrast, brains in Group III contained a dense network of 6.423-immunoreactive (IR) thread-like structures ("ghost" neurites) and plaque-like structures with granular appearance, in addition to NFT. The number of 6.423-IR structures appeared to be related to the duration of clinical dementia and the age of onset. Furthermore, "ghost" neurites were more abundant in young AD cases. The possible significance of the 6.423-IR pattern in the pathogenesis of AD is discussed.

8/7/198 (Item 55 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01092219 Genuine Article#: FV816 Number of References: 52
Title: EPITOPE MAP OF NEUROFILAMENT PROTEIN DOMAINS IN CORTICAL AND
PERIPHERAL NERVOUS-SYSTEM LEWY BODIES
Author(s): SCHMIDT ML; MURRAY J; LEE VMY; HILL WD; WERTKIN A; TROJANOWSKI
JQ
Corporate Source: HOSP UNIV PENN,DIV ANAT PATHOL,MALONEY BLDG BASEMENT,ROOM
A009,3400 SPRUCE ST/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED,DEPT
PATHOL & LAB MED,DIV ANAT PATHOL/PHILADELPHIA//PA/19104; UNIV PENN,SCH
MED,DEPT ANAT/PHILADELPHIA//PA/19104
Journal: AMERICAN JOURNAL OF PATHOLOGY, %%%1991%%%, V139, N1, P53-65
Language: ENGLISH Document Type: ARTICLE
Abstract: A subset of demented elderly patients exhibit large numbers of cortical intraneuronal inclusions similar to the neurofilament (NF)-rich Lewy bodies (LB) found in pigmented subcortical neurons of patients with Parkinson's disease (PD). Because these cortical inclusions may contribute to the emergence of cognitive impairments in afflicted individuals, the authors mapped the distribution of NF epitopes in these so-called cortical LBs. This was done using ethanol-fixed tissues and a large library of monoclonal antibodies (MAbs) with well-characterized binding specificities to various regions of each NF triplet protein. Cortical LBs were examined by light, confocal, and electron microscopy, and they were compared with the subcortical LBs of PD and LBs in the peripheral nervous system (PNS). Monoclonal antibodies specific for the rod regions of each of the three NF subunits, or for phosphate-dependent and independent antigenic sites in the tail region of the high-(NF-H) and middle- (NF-M) molecular weight (M(r)) NF subunits as well as other MAbs to the extreme COOH terminus of NF-L and NF-M or the head region of NF-M labeled a variable number of cortical LBs. Remarkably one of these anti-NF MAbs, RMO32, which recognized a %%%phosphorylated%%% epitope in the tail region of NF-M, immunolabeled nearly all cortical LBs, whereas each of the other anti-NF MAbs never labeled more than 10% of ubiquitin- or RMO32-positive cortical LBs. Further LBs in the PNS resembled those in the central nervous system (CNS) in their immunologic properties, and LBs in both sites were dominated by filamentous aggregates at the ultrastructural level. These findings suggest that NF proteins are profoundly altered during their incorporation into cortical and PNS LBs. Further the authors here identified immunologic and ultrastructural properties common to cortical LBs, PNS LBs, and classic substantia nigra LBs in PD. The accumulation of filamentous, perikaryal inclusions rich in NF proteins at diverse sites in the CNS and PNS of patients with a variety of neurodegenerative disorders suggests a widespread disruption of NF metabolism or transport.

8/7/199 (Item 56 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01079585 Genuine Article#: FU901 Number of References: 44
Title: DIFFERENCE BETWEEN THE %%%TAU%%%-PROTEIN OF %%%ALZHEIMER%%% PAIRED
HELICAL FILAMENT CORE AND NORMAL %%%TAU%%% REVEALED BY EPITOPE ANALYSIS
OF MONOCLONAL ANTIBODIES-423 AND ANTIBODIES-7.51
Author(s): NOVAK M; JAKES R; EDWARDS PC; MILSTEIN C; WISCHIK CM
Corporate Source: MRC,MOLEC BIOL LAB,HILLS RD/CAMBRIDGE CB2 2QH//ENGLAND/;
UNIV CAMBRIDGE,DEPT PSYCHIAT,CTR MRC,CAMBRIDGE BRAIN BANK LAB/CAMBRIDGE
CB2 2QH//ENGLAND/
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED
STATES OF AMERICA, %%%1991%%%, V88, N13, P5837-5841
Language: ENGLISH Document Type: ARTICLE
Abstract: The microtubule-associated protein %%%tau%%% that is incorporated
into paired helical filaments (PHFs) undergoes some form of aberrant posttranslational processing in %%%Alzheimer%%% disease. Difficulties in deciding which changes are critical for PHF formation stem in part from the lack of immunochemical markers specific for PHF %%%tau%%%. The
only monoclonal antibody (mAb) that is known to react with PHF %%%tau%%% but not with the predominant normal adult %%%tau%%% species
is mAb 423. Another mAb (7.51, described in this paper) recognizes a segment of %%%tau%%% that is included in the minimal recognition unit required by mAb 423. Unlike 423, which is PHF %%%tau%%%-specific, mAb
7.51 recognizes all PHF core-derived %%%tau%%% as well as native soluble %%%tau%%% and recombinant %%%tau%%% expressed in bacteria and
so serves as a generic %%%tau%%% marker. Both epitopes are in the 12-kDa fragment released from the Pronase-resistant core of the PHF (which encompasses the tandem repeat region). The mAb 7.51 epitope requires segments located in the last two repeats, which are common to all %%%tau%%% isoforms. The mAb 423 epitope requires sequences located
near both the N and the C terminus of the 12-kDa fragment common to three- and four-repeat %%%tau%%% isoforms. Fragments denatured by concentrated formic acid and SDS regain 423 reactivity when denaturing agents are removed. Since the primary amino acid sequences of PHF %%%tau%%% and normal %%%tau%%% are identical in the repeat region, we
conclude that 423 reactivity also requires a modification(s) occurring within an almost-equal-to 90-residue segment that are not present in %%%tau%%% proteins so far described in the human brain.

8/7/200 (Item 57 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01005645 Genuine Article#: FN312 Number of References: 45
Title: GROWTH CONES - THE MECHANISM OF NEURITE ADVANCE
Author(s): GORDONWEEKS PR
Corporate Source: UNIV LONDON KINGS COLL,DIV BIOMED SCI,ANAT & HUMAN BIOL
GRP,THE STRAND/LONDON WC2R 2LS//ENGLAND/
Journal: BIOESSAYS, %%%1991%%%, V13, N5, P235-239
Language: ENGLISH Document Type: REVIEW
Abstract: Growth cones are the highly motile structures found at the tips of growing axons and dendrites (neurites), which extend from neurones, during the development of the nervous system. They function both as detectors and transducers of extrinsic guidance cues and as regions where the neurite cytoskeleton is assembled. Without concerted neurite assembly, advance cannot occur. Assembly of the neurite cytoskeleton in growing neurites chiefly involves microtubule assembly at the growth cone. Some of the factors that may influence microtubule assembly in growth cones are becoming apparent and include post-translational modification of tubulin itself and microtubule associated proteins, particularly %%%tau%%% and MAP1B.

8/7/201 (Item 58 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01002020 Genuine Article#: FM522 Number of References: 45
Title: STRUCTURAL STABILITY OF PAIRED HELICAL FILAMENTS REQUIRES

MICROTUBULE-BINDING DOMAINS OF %%%TAU%%% - A MODEL FOR SELF-ASSOCIATION
Author(s): KSIEZAKREDING H; YEN SH
Corporate Source: YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT PATHOL/BRONX//NY/10461
Journal: NEURON, %%%1991%%%, V6, N5, P717-728
Language: ENGLISH Document Type: ARTICLE
Abstract: Highly purified and SDS-soluble paired helical filaments (PHFs) were immunogold labeled and immunoblotted with antibodies to %%%tau%%%:
%%%Tau%%% 14 (N-terminal half), AH-1 (microtubule-binding domain), and
%%%Tau%%% 46 (C-terminal end). The main component of PHFs was modified
%%%tau%%% of 68, 64, and 60 kd, also called A68 or PHF-%%%tau%%%. Trypsin digestion reduced the maximum width of PHFs by 10%-20%, increased aggregation of filaments, and abolished the binding of %%%Tau%%% 14, but had no effect on the binding of AH-1. The smallest %%%tau%%%-reactive tryptic fragments were 13 and 7-8 kd, positive with
AH-1, and negative with %%%Tau%%% 46. Our results and the model of Crowther and Wischik suggest that by self-association and anti-parallel arrangement of the microtubule-binding domains, PHF-%%%tau%%% forms the
backbone of PHFs.

8/7/202 (Item 59 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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00971615 Genuine Article#: FK902 Number of References: 14
Title: EFFECT OF MAP2, MAP2C, AND %%%TAU%%% ON KINESIN-DEPENDENT
MICROTUBULE MOTILITY
Author(s): HEINS S; SONG YH; WILLE H; MANDELKOW E; MANDELKOW EM
Corporate Source: DESY,MAX PLANCK UNIT STRUCT MOLEC BIOL,NOTKESTR85/D-2000
HAMBURG 52//FED REP GER/; DESY,MAX PLANCK UNIT STRUCT MOLEC
BIOL,NOTKESTR85/D-2000 HAMBURG 52//FED REP GER/
Journal: JOURNAL OF CELL SCIENCE, %%%1991%%%, S14, P121-124
Language: ENGLISH Document Type: ARTICLE
Abstract: By making use of DIC video microscopy to monitor microtubule motility we have studied the effect of several MAPs (MAP2, MAP2c, %%%tau%%%) on microtubule-kinesin interactions and microtubule gliding. Of the three MAPs tested, MAP2 interferes most strongly with kinesin-dependent microtubule motility.

8/7/203 (Item 60 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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00952498 Genuine Article#: FJ499 Number of References: 60
Title: MOLECULAR CHARACTERIZATION OF MICROTUBULE-ASSOCIATED PROTEINS-
%%%TAU%%% AND MAP2
Author(s): GOEDERT M; CROWTHER RA; GARNER CC
Corporate Source: MRC,MOLEC BIOL LAB,HILLS RD/CAMBRIDGE CB2 2QH//ENGLAND/;
UNIV HAMBURG,CTR MOLEC NEUROBIOL/D-2000 HAMBURG20//FED REP GER/
Journal: TRENDS IN NEUROSCIENCES, %%%1991%%%, V14, N5, P193-199
Language: ENGLISH Document Type: REVIEW
Abstract: %%%Tau%%% and MAP2 are two of the major microtubule-associated
proteins in the vertebrate nervous system. They promote microtubule assembly and stability, and might be involved in the establishment and maintenance of neuronal polarity. In nerve cells immunohistochemistry shows complementary distributions, with %%%tau%%% being concentrated in
axons and high molecular mass MAP2 being confined to dendrites. Each protein consists of multiple isoforms that contain three or four homologous tandem repeats near the carboxy-terminus, which constitute microtubule-binding domains. In humans, %%%tau%%% consists of at least
six isoforms of related amino acid sequences that are produced from a single gene by alternative mRNA splicing and that are expressed in a stage- and cell type-specific manner. %%%Tau%%% is also a component of
the paired helical filaments associated with %%%Alzheimer%%%'s disease
and other disorders of the CNS. Rat MAP2 consists of at least three isoforms produced from a single gene: high molecular mass MAP2a and MAP2b, and low molecular mass MAP2c. MAP2c is expressed only during early development and has so far been seen only in axons; MAP2a appears to replace MAP2c, whereas MAP2b is expressed throughout life. Messenger RNAs for MAP2 of high molecular mass are expressed both in cell bodies and in dendrites, consistent with the dendritic localization of the corresponding protein isoforms.

8/7/204 (Item 61 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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00816606 Genuine Article#: EY528 Number of References: 19
Title: THE DECREASED LEVEL OF CASEIN KINASE-2 IN BRAIN CORTEX OF
SCHIZOPHRENIC AND %%%ALZHEIMERS%%%-DISEASE PATIENTS
Author(s): AKSENOVA MV; BURBAEVA GS; KANDROR KV; KAPKOV DV; STEPANOV AS
Corporate Source: ACAD MED SCI USSR,ALL UNION RES CTR MENTAL HLTH,ZAGORODNOE SHOSSE 2/MOSCOW 109801//USSR/; AN BAKH BIOCHEM
INST/MOSCOW//USSR/
Journal: FEBS LETTERS, %%%1991%%%, V279, N1, P55-57
Language: ENGLISH Document Type: ARTICLE
Abstract: The content of casein kinase 2 is considerably decreased in ribosome-free extracts of the frontal cortex of schizophrenic and %%%Alzheimer%%%'s disease patients in comparison to normal brains as has been demonstrated by means of immunoblotting. The activity of casein kinase 2 towards endogenous substrates and casein is also diminished in the cases of mental pathologies examined. This phenomenon may explain the well-known aberrations in the %%%phosphorylation%%% of structural proteins of human brain which are
intrinsic for the mental diseases.

8/7/205 (Item 62 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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00777993 Genuine Article#: EW029 Number of References: 49
Title: NONNEURONAL 210X103 MR MICROTUBULE-ASSOCIATED PROTEIN (MAP4)
CONTAINS A DOMAIN HOMOLOGOUS TO THE MICROTUBULE-BINDING DOMAINS OF
NEURONAL MAP2 AND %%%TAU%%%
Author(s): CHAPIN SJ; BULINSKI JC
Corporate Source: COLUMBIA UNIV COLL PHYS & SURG,DEPT ANAT & CELLBIOL,BB-1213,630 W 168TH ST/NEW YORK//NY/10032; UNIV CALIF LOS
ANGELES/LOS ANGELES//CA/90024
Journal: JOURNAL OF CELL SCIENCE, %%%1991%%%, V98, JAN, P27-36
Language: ENGLISH Document Type: ARTICLE

8/7/206 (Item 63 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

00770569 Genuine Article#: EV366 Number of References: 50
Title: CHARACTERIZATION AND DIFFERENTIAL DISTRIBUTION OF THE 3 MAJOR HUMAN
PROTEIN-KINASE-C ISOZYMES (PKC-ALPHA, PKC-BETA, AND PKC-GAMMA) OF THE
CENTRAL-NERVOUS-SYSTEM IN NORMAL AND %%%ALZHEIMERS%%%-DISEASE BRAINS

Author(s): CLARK EA; LEACH KL; TROJANOWSKI JQ; LEE VMY
Corporate Source: HOSP UNIV PENN,SCH MED,DEPT PATHOL & LAB MED,MALONEY
BASEMENT,ROOM A009,36TH & SPRUCE ST/PHILADELPHIA//PA/19104; UNIV
PENN,SCH MED,DEPT PATHOL & LAB MED/PHILADELPHIA//PA/19104; UNIV
PENN,SCH MED,CELL BIOL GRAD GRP/PHILADELPHIA//PA/19104; UPJOHN CO,DEPT
CELL BIOL/KALAMAZOO//MI/49001
Journal: LABORATORY INVESTIGATION, %%%1991%%%, V64, N1, P35-44
Language: ENGLISH Document Type: ARTICLE

8/7/207 (Item 64 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

00755885 Genuine Article#: EU328 Number of References: 34
Title: %%%TAU%%% IN %%%ALZHEIMER%%% NEUROFIBRILLARY TANGLES - N-TERMINAL
AND C-TERMINAL REGIONS ARE DIFFERENTIALLY ASSOCIATED WITH PAIRED
HELICAL FILAMENTS AND THE LOCATION OF A PUTATIVE ABNORMAL
%%%PHOSPHORYLATION%%% SITE
Author(s): BRION JP; HANGER DP; BRUCE MT; COUCK AM; FLAMENTDURAND J;
ANDERTON BH
Corporate Source: UNIV LIBRE BRUXELLES,ANAT PATHOL & MICROSCOPIE ELECTRON
LAB,808 ROUTE LENNIK,BLDG C-10/B-1070 BRUSSELS//BELGIUM/; INST
PSYCHIAT/LONDON SE5 8AF//ENGLAND/
Journal: BIOCHEMICAL JOURNAL, %%%1991%%%, V273, JAN, P127-133
Language: ENGLISH Document Type: ARTICLE

8/7/208 (Item 65 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

00754226 Genuine Article#: ET968 Number of References: 19
Title: TYROSINE %%%PHOSPHORYLATION%%% SYSTEMS IN %%%ALZHEIMERS%%%-DISEASE
PATHOLOGY
Author(s): WOOD JG; ZINSMEISTER P
Corporate Source: EMORY UNIV,SCH MED,DEPT ANAT & CELL BIOL/ATLANTA//GA/30322; OGLETHORPE UNIV,DEPT BIOL/ATLANTA//GA/00000
Journal: NEUROSCIENCE LETTERS, %%%1991%%%, V121, N1-2, P12-16
Language: ENGLISH Document Type: ARTICLE

8/7/209 (Item 66 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.

00582386 Genuine Article#: ED922 Number of References: 26
Title: %%%PHOSPHORYLATION%%% OF MICROTUBULE-ASSOCIATED PROTEIN-%%%TAU%%% -
IDENTIFICATION OF THE SITE FOR CA-2+-CALMODULIN DEPENDENT KINASE AND
RELATIONSHIP WITH %%%TAU%%%-%%%PHOSPHORYLATION%%% IN %%%ALZHEIMER%%%
TANGLES
Author(s): STEINER B; MANDELKOW EM; BIERNAT J; GUSTKE N; MEYER HE; SCHMIDT
B; MIESKES G; SOLING HD; DRECHSEL D; KIRSCHNER MW; GOEDERT M; MANDELKOW
E
Corporate Source: DESY,MAX PLANCK UNIT STRUCT MOLEC BIOL,NOTKESTR85/D-2000
HAMBURG 52//FED REP GER/; DESY,MAX PLANCK UNIT STRUCT MOLEC BIOL,NOTKESTR85/D-2000 HAMBURG 52//FED REP GER/; RUHR UNIV BOCHUM,INST
PHYSIOL CHEM/D-4630 BOCHUM//FED REP GER/; UNIV GOTTINGEN,DEPT BIOCHEM
2/D-3400 GOTTINGEN//FED REP GER/; UNIV GOTTINGEN,INST CLIN
BIOCHEM/D-3400 GOTTINGEN//FED REP GER/; UNIV CALIF SAN FRANCISCO,SCH
MED,DEPT BIOCHEM &BIOPHYS/SAN FRANCISCO//CA/94143; MRC,MOLEC BIOL
LAB/CAMBRIDGE CB2 2QH//ENGLAND/
Journal: EMBO JOURNAL, %%%1990%%%, V9, N11, P3539-3544
Language: ENGLISH Document Type: ARTICLE

8/7/210 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2002 Elsevier Science B.V. All rts. reserv.

05211622 EMBASE No: 1992351856
Differential %%%phosphorylation%%% of %%%tau%%% by cyclic AMP-dependent
protein kinase and Casup 2sup +/calmodulin-dependent protein kinase II: Metabolic and functional consequences
Johnson G.V.W.
Sparks Center, University of Alabama,Birmingham, AL 35294-0017 United States
Journal of Neurochemistry (J. NEUROCHEM.) (United States) 1992, 59/6
(2056-2062)
CODEN: JONRA ISSN: 0022-3042
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The effects of cyclic AMP-dependent protein kinase (cAMP-PK) or Casup 2sup +/calmodulin-dependent protein kinase II (CaMKII) %%%phosphorylation%%% on the binding of bovine %%%tau%%% to tubulin and
calpain-mediated degradation of %%%tau%%% were studied. Both cAMP-PK and
CaMKII readily %%%phosphorylated%%% %%%tau%%% and slowed the migration of
%%%tau%%% on sodium dodecyl sulfate-containing polyacrylamide gels. However, cAMP-PK %%%phosphorylated%%% %%%tau%%% to a significantly greater
extent than CaMKII (1.5 and 0.9 mol of sup 3sup 2P/mol of %%%tau%%%, respectively), and %%%phosphorylation%%% of %%%tau%%% by cAMP-PK resulted
in a greater shift to a more acidic, less heterogeneous pattern on two-dimensional nonequilibrium pH gradient gels compared with CaMKII %%%phosphorylation%%%. Two-dimensional phosphopeptide maps indicate that
cAMP-PK %%%phosphorylates%%% a site or sites on %%%tau%%% that are %%%phosphorylated%%% by CaMKII, as well as a unique site or sites that are
not %%%phosphorylated%%% by CaMKII. %%%Phosphorylation%%% of %%%tau%%% by
cAMP-PK significantly decreased tubulin binding and, as previously reported, also inhibited the calpain-induced degradation of %%%tau%%%. CaMKII %%%phosphorylation%%% of %%%tau%%% did not alter either of these
parameters. These results suggest that the %%%phosphorylation%%% of site(s)
on the %%%tau%%% molecule uniquely accessible to cAMP-PK contributed to the
decreased %%%tau%%%-tubulin binding and increased resistance to calpain hydrolysis.

8/7/211 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
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05205388 EMBASE No: 1992345622
A serine <rt arrow> proline change in the %%%Alzheimer%%%'s disease-associated epitope %%%Tau%%% 2 results in altered secondary

structure, but %%%phosphorylation%%% overcomes the conformational gap
Lang E.; Otvos Jr. L.
Wistar Institute of Anatomy/Biology, 3601 Spruce Street,Philadelphia, PA 19104 United States
Biochemical and Biophysical Research Communications (BIOCHEM. BIOPHYS. RES. COMMUN.) (United States) 1992, 188/1 (162-169)
CODEN: BBRCA ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Monoclonal antibody %%%Tau%%% 2 was raised against bovine %%%tau%%% protein, was reported to recognize a conformational epitope, and stained %%%tau%%% was found in neurofibrillary tangles of %%%Alzheimer%%%'s disease, but not normal human %%%tau%%%. We synthesized tetradeka peptides corresponding to the original bovine sequence, its serine <rt arrow> proline substituted analog, the genuine human sequence of this region, and the bovine epitope %%%phosphorylated%%% on the crucial serine. The secondary structure of the peptides was determined by circular dichroism. It was found that only the original bovine epitope showed a tendency to form the beta-pleated sheets characteristic of the neurofibrillary tangles. The spectra of the human peptide, its analog, and the %%%phosphorylated%%% bovine sequence were very similar, featuring a weak, helical beta-turn character. Eventual %%%phosphorylation%%% of epitopes of this otherwise heavily %%%phosphorylated%%% protein may overcome inter-species conformational gaps.

8/7/212 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
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05189598 EMBASE No: 1992329832
p42 map kinase %%%phosphorylation%%% sites in microtubule-associated protein %%%tau%%% are dephosphorylated by protein phosphatase 2Ainf 1. Implications for %%%Alzheimer%%%'s disease
Goedert M.; Cohen E.S.; Jakes R.; Cohen P.
MRC Laboratory of Molecular Biology, Hills Road,Cambridge CB2 2QH United Kingdom
FEBS Letters (FEBS LETT.) (Netherlands) 1992, 312/1 (95-99)
CODEN: FEBLA ISSN: 0014-5793
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The paired helical filament (PHF), which comprises the major fibrous element of the neurofibrillary tangle of %%%Alzheimer%%%'s disease, is composed of abnormally %%%phosphorylated%%% microtubule-associated protein %%%tau%%%. Here we show that p42 MAP kinase %%%phosphorylates%%% recombinant %%%tau%%% and converts it to a form which is similar to PHF %%%tau%%%. Of the major serine/threonine protein phosphatases found in mammalian tissues only protein phosphatase 2A (PP2A) could dephosphorylate %%%tau%%% %%%phosphorylated%%% in this manner, with PP2Ainf 1 being the most effective form of the enzyme.

8/7/213 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
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04893991 EMBASE No: 1992034206
In situ hybridization of calcium/calmodulin dependent protein kinase II and %%%tau%%% mRNAs: Species differences and relative preservation in %%%Alzheimer%%%'s disease
Mah V.H.; Eskin T.A.; Kazee A.M.; Lapham L.; Higgins G.A.
Department of Neurobiology and Anatomy, University of Rochester Medical Center, Rochester, NY 14642 United States
Molecular Brain Research (MOL. BRAIN RES.) (Netherlands) 1992, 12/1-3 (85-94)
CODEN: MBREE ISSN: 0169-328X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Abnormal %%%phosphorylation%%% of the microtubule associated protein %%%tau%%% component of neurofibrillary tangles (NPTs) in %%%Alzheimer%%%'s disease (AD) may result from alterations in protein kinase expression. Calcium/calmodulin dependent protein kinase II (CaM kinase II) has been shown to %%%phosphorylate%%% %%%tau%%% in vitro in such a way to decrease its electrophoretic mobility. A68, apparently a modified form of %%%tau%%% in AD brain, also shows abnormal %%%phosphorylation%%% and slower mobility than %%%tau%%%. To further examine the role of CaM kinase II in AD, in situ hybridization studies were performed on tissues from rat, monkey and human to examine and compare the patterns of CaM kinase II mRNA expression in different brain regions. The most notable differences among the three species were observed in dendrites in layer I of isocortex, in the molecular layer of the dentate gyrus and stratum radiatum and stratum lacunosum-moleculare in hippocampus, where hybridization was detected in rat, but not in monkey or human brain. In addition, comparisons between %%%tau%%% and CaM kinase II mRNA expression were made in tissue from normal aged adults and AD patients, especially in areas prone to NFT formation. CaM kinase II and %%%tau%%% mRNAs were co-expressed in many neuronal populations, both those which are prone to NPT formation as well as those which are rarely affected by AD changes. No major differences in the relative abundance of either CaM kinase II or %%%tau%%% mRNA within particular neuronal populations was noted between normal aged and AD brain. Diminished hybridization was associated with serve neuronal pathology and cell loss.

8/7/214 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE
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04748113 EMBASE No: 1991241467
Hydrated autoclave pretreatment enhances %%%TAU%%% immunoreactivity in formalin-fixed normal and %%%Alzheimer%%%'s disease brain tissues
Shin R.-W.; Iwaki T.; Kitamoto T.; Tateishi J.
Dept. Neuropathology/Neurology, Neurological Institute, Kyushu University 60, Maidashi,Higashi-ku, Fukuoka 812 Japan
Laboratory Investigation (LAB. INVEST.) (United States) 1991, 64/5 (693-702)
CODEN: LAINA ISSN: 0023-6837
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We developed a new immunohistochemical method by which normal %%%tau%%% antigenicity can be visualized in paraffin sections of formalin-fixed brain tissue. This method consists of autoclave pretreatment of sections immersed into distilled water (hydrated autoclaving) before incubation with anti-%%%tau%%% antibodies. In normal human brain, immunoreactive %%%tau%%% was detected in neuronal cell bodies and dendrites, axon fibers, astroglia, oligodendroglia and gray matter neuropil. In previous studies on normal %%%tau%%% distribution, different optimized fixations that effectively preserve %%%tau%%% antigenicity were used but none of these revealed all of these compartments together. Our method is therefore considered to be more sensitive for detecting normal %%%tau%%% immunoreactivity. In addition, hydrated autoclaving had an enhancing effect on the abnormally %%%phosphorylated%%% (modified) %%%tau%%% immunoreactivity in formalin-fixed brains. In hydrated autoclaving of sections from patients with %%%Alzheimer%%%'s disease, neuropil threads, senile plaques, extracellular and intracellular tangles were enhanced in quantity and in

staining intensity. Therefore, modified %%%tau%%% appears to accumulate more densely than expected from conventional immunohistochemistry. Immunoblot analysis showed that normal or modified %%%tau%%% immunoreactivity was totally or partially eliminated on formalin treatment and could be revisualized by hydrated autoclaving, an event presumably related to recovering of formalin-masked %%%tau%%% antigens through denaturation by hydrated autoclaving.

8/7/215 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

04710244 EMBASE No: 1991203598
Pathology of %%%Alzheimer%%%'s disease
Blass J.P.; Ko L.-W.; Wisniewski H.M.
The Burke Rehabilitation Center, 785 Mamaroneck Avenue, White Plains, NY
10605 United States
Psychiatric Clinics of North America (PSYCHIATR. CLIN. NORTH AM.) (United States) 1991, 14/2 (397-420)
CODEN: PCAMD ISSN: 0193-953X
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The fundamental pathophysiology of %%%Alzheimer%%%'s disease remains poorly understood, but progress has been dramatic in description of the pathology at the molecular level. The characteristic %%%Alzheimer%%% amyloid derives, in part, by action of microglia, from a precursor protein that is well characterized at the protein and gene levels. The characteristic paired helical filaments contain %%%phosphorylated%%% %%%tau%%% proteins and perhaps other constituents. At the neurotransmitter
level, %%%Alzheimer%%%'s disease involves not only loss of cholinergic cells but of serotonergic and other neurotransmitter systems as well. Damage to mitochondria may play an important role in precipitating the cellular pathophysiology.

8/7/216 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

04544064 EMBASE No: 1991038107
%%%Tau%%% in %%%Alzheimer%%% neurofibrillary tangles. N- and C-terminal
regions are differentially associated with paired helical filaments and the location of a putative abnormal %%%phosphorylation%%% site
Brion J.-P.; Hanger D.P.; Bruce M.T.; Couck A.-M.; Flament-Durand J.; Anderton B.H.
Laboratoire d'Anatomie Pathol., Universite Libre de Bruxelles, 808 Route de Lennik,1070-Brussels Belgium
Biochemical Journal (BIOCHEM. J.) (United Kingdom) 1991, 273/1 (127-133)
CODEN: BIJOA ISSN: 0264-6021
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

To investigate the extent to which whole %%%tau%%% proteins, structurally
abnormal %%%tau%%% and fragments of %%%tau%%% are incorporated into
neurofibrillary tangles in %%%Alzheimer%%%'s disease, an immunocytochemical
mapping study using a panel of antibodies to several synthetic human %%%tau%%% peptides has been performed. Neurofibrillary tangles were immunolabelled in situ, and paired helical filaments (PHF), the principle structural component of tangles, were immunolabelled after isolation and Pronase treatment. N-Terminal and C-terminal domains of %%%tau%%% were
found to be present in tangles in situ. SDS-treated PHF were found to contain most of the C-terminal half of %%%tau%%% and were also labelled by
antibodies to ubiquitin. Only some of these PHF were labelled by antisera to %%%tau%%% sequences towards the N-terminus, and this enabled the identification of a region of %%%tau%%% in which proteolytic cleavage may occur. The ultrastructural appearance of the immunolabelling suggested that both the N- and C-terminal domains of %%%tau%%% extend outwards from the
axis of PHF. After Pronase treatment, PHF were strongly labelled only by an antiserum to PHF and by the antiserum to the most C-terminal %%%tau%%% synthetic peptide. The latter antiserum also strongly labelled
extracellular tangles in situ, whereas these extracellular tangles were poorly labelled by the antisera to the other synthetic peptides. One anti-(%%%tau%%% peptide) serum labelled a population of neurofibrillary tangles in situ only after alkaline phosphatase pretreatment of tissue sections. Our results show that, although peptides along the length of the %%%tau%%%
molecule are associated with neurofibrillary tangles in situ, only the C-terminal one-third of the molecule is tightly associated with PHF, since this region of %%%tau%%% is resistant to SDS treatment of PHF. We also report the existence in PHF in situ of a masked %%%tau%%% epitope which is
partially unmasked by dephosphorylation. These results are indicative of post-translational changes in tangle-associated %%%tau%%% in degenerating
neurons in %%%Alzheimer%%%'s disease.

8/7/217 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

04455185 EMBASE No: 1990343294
%%%Phosphorylation%%% of microtubule-associated protein %%%tau%%%:
Identification of the site for Casup 2sup +-calmodulin dependent kinase and relationship with %%%tau%%% %%%phosphorylation%%% in %%%Alzheimer%%%
tangles
Steiner B.; Mandelkow E.-M.; Biernat J.; Gustke N.; Meyer H.E.; Schmidt B.; Mieskes G.; Soling H.D.; Drechsel D.; Kirschner M.W.; Goedert M.; Mandelkow E.
Max-Planck-Unit for, Structural Molecular Biology, c/o DESY, Notkestrasse
85,D-2000 Hamburg 52 Germany
EMBO Journal (EMBO J.) (United Kingdom) 1990, 9/11 (3539-3544)
CODEN: EMJOD ISSN: 0261-4189
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The microtubule array in neuronal cells undergoes extensive growth, dynamics and rearrangements during neurite outgrowth. While little is known about how these changes are regulated, microtubule-associated proteins (MAPs) including %%%tau%%% protein are likely to perform an important role.
%%%Tau%%% is one of the MAPs in mammalian brain. When isolated it is usually a mixture of several isoforms containing between 341 and 441 residues that arise from alternative splicing. %%%Tau%%% can be %%%phosphorylated%%% by several protein kinases. %%%Phosphorylation%%% at
certain sites results in major structural and functional changes, as seen by changes in electrophoretic mobility, interaction with microtubules, molecular length and elasticity. Here we show that the sites of %%%phosphorylation%%% by four kinases (PKA, PKC, CK and CaMK) all lie in the C-terminal microtubule-binding half of %%%tau%%%, but only the %%%phosphorylation%%% by CaM kinase shows the pronounced shift in electrophoretic mobility characteristic for %%%tau%%% from %%%Alzheimer%%%
neurofibrillary tangles. By using a combination of limited proteolysis, protein sequencing and protein engineering we show that a single %%%phosphorylation%%% site is responsible for this shift, located at Ser 405 in the C-terminal tail of the protein outside the region of internal repeats. %%%Phosphorylation%%% at this site not only reduces the electrophoretic mobility of %%%tau%%%, it also makes the protein long and stiff, as shown earlier. The site is likely to be %%%phosphorylated%%% in %%%tau%%% from %%%Alzheimer%%% neurofibrillary tangles.

8/7/218 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

04076430 EMBASE No: 1989245476
Cytoskeletal protein pathology and the formation of beta-amyloid fibers in %%%Alzheimer%%%'s disease
Wisniewski H.M.; Iqbal K.; Bancher C.; Miller D.; Currie J.
New York Office of Mental Retardation and Developmental Disabilities, Staten Island, NY United States
Neurobiology of Aging (NEUROBIOL. AGING) (United States) 1989, 10/5
(409-412)
CODEN: NEAGD ISSN: 0197-4580
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Discovery of the abnormally %%%phosphorylated%%% %%%tau%%% in paired
helical filaments, its accumulation preceding the formation of the tangles and the in vitro microtubule assembly defect suggest that an abnormality in the protein %%%phosphorylation%%%/dephosphorylation system is involved in
the pathogenesis of %%%Alzheimer%%% cytoskeletal pathology. The levels of
mRNA for the beta-amyloid precursor protein (betaAPP) in the brain suggest
that only a small deficiency in the processing of the precursor would be sufficient to account for the accumulation of beta-amyloid in %%%Alzheimer%%% brain. Identification of reticuloendothelial system cells responsible for the production/processing of beta-amyloid will help to elucidate the pathogenesis of the brain amyloidosis. The disproportionate accumulation of paired helical filaments and amyloid within the same affected brain and from disease raises the possibility of different etiologies for each of these lesions coexisting in %%%Alzheimer%%%'s disease.

8/7/219 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

03970272 EMBASE No: 1989139268
The reinterpretation of the immunochemical study of %%%Alzheimer%%% neurofibrillary tangles
Nukina N.
Center for Neurologic Diseases, Harvard Medical School, Boston, MA 02115 United States
Annals of Medicine (ANN. MED.) (Finland) 1989, 21/2 (117-119)
CODEN: ANMDE ISSN: 0785-3890
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Many studies have been done on neurofibrillary tangles occurring in %%%Alzheimer%%%'s disease using antibodies, but without agreement on the
interpretation of the results. Immunochemical studies using antibodies to neurofilament and %%%tau%%% and the antibody, Alz50, were carried out to
establish a common view. The results suggest that: 1) antibodies to neurofilament recognizing tangles react with the %%%phosphorylated%%% epitope of %%%tau%%% in paired helical filaments; 2) Alz50 reacts with abnormal %%%tau%%%, which has slower electrophoretic mobility than normal
%%%tau%%%; and 3) a certain part of %%%tau%%% has the protease-resistant
property in brains affected by the disease.

8/7/220 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

03970271 EMBASE No: 1989139267
Selective expression of epitopes in multiphosphorylation repeats of the high and middle molecular weight neurofilament proteins in %%%Alzheimer%%%
neurofibrillary tangles
Trojanowski J.Q.; Schmidt M.L.; Otvos Jr. L.; Gur R.C.; Gur R.E.; Hurtig H.; Lee V.M.Y.
Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Hospital of University of Pennsylvania, Philadelphia, PA 19104-4283 United States
Annals of Medicine (ANN. MED.) (Finland) 1989, 21/2 (113-116)
CODEN: ANMDE ISSN: 0785-3890
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Here we review our recent 'epitope analyses' of a few of the fibrous intraneuronal inclusions that are distinctive hallmarks of human neurodenerative conditions using a large library of monoclonal antibodies (MAbs) raised to normal neuronal cytoskeletal proteins. Analyses of the low (NF-L), middle (NF-M), and high (NF-H) molecular weight neurofilament (NF) proteins with > 500 MAbs enumerated epitopes shared by NF proteins and the
intraneuronal neurofibrillary tangles (NFTs) that occur in the hippocampus and brainstem of %%%Alzheimer%%%'s disease (AD) subjects. We identified the
NF-H multi-%%%phosphorylation%%% repeat domain, i.e. repeats of Lys-Ser-Pro-X (where X is a small uncharged amino acid and Ser acts as a phosphate acceptor), as the determinant recognized by 15/16 MAbs that detected NFTs in sections of AD hippocampus, and 11 of the same 16 MAbs recognised NF-M multi-%%%phosphorylation%%% repeats. Further, the antigen
binding regions of these MAbs were shown to comprise 13 separate classes based on their differential binding to 12 synthetic peptides derived from the NF-H and NF-M multi-%%%phosphorylation%%% sites, NF subunits of 10
diverse mammalian and sub-mammalian species, and normal human %%%tau%%% (
%%%tau%%%). None of these anti-NF MAbs recognized NFTs in the brainstem of
subjects with progressive supranuclear palsy (PSP), but NFTs in AD brainstem sections were reactive with five of these MAbs. Both PSP and AD brainstem NFTs were recognized by MAbs specific for %%%tau%%% and paired
helical filament antigens. Hirano bodies (HBs), another intraneuronal inclusion in the hippocampus of AD and non-AD subjects, were immunostained
by 4 anti-NF MAbs, but none of these MAbs were specific for the NF-H and NF-M multi-%%%phosphorylation%%% repeats. These studies indicate that NF-H
and NF-M multi-%%%phosphorylation%%% repeats are the most likely sequences
in NF-H and NF-M present in NFTs, while %%%tau%%%-like determinants are
more substantially represented in both AD and PSP NFTs. In contrast, HBs are immunologically distinct from NFTs. Thus, different pathological events are likely to account for the formation of each of these distinct lesions.

8/7/221 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

03960296 EMBASE No: 1989129289
Abnormal %%%tau%%% species are produced during %%%Alzheimer%%%'s disease
neurodegenerating process
Flament S.; Delacourte A.
Unite INSERM no. 16, Faculte de Medecine, Laboratoire de Neurosciences, 59045 Lille France
FEBS Letters (FEBS LETT.) (Netherlands) 1989, 247/2 (213-216)
CODEN: FEBLA ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

%%%Tau%%% proteins were detected in human brain using two polyclonal antibodies: anti-paired helical filaments and anti-human native %%%tau%%% proteins. Both antisera detected identically the normal set of %%%tau%%% proteins in control brains. Moreover they detected two abnormal %%%tau%%%
variants of 64 and 69 kDa exclusively in brain areas showing neurofibrillary tangles and senile plaques. %%%Tau%%% 64 and 69 were abnormally %%%phosphorylated%%% as revealed by the decrease in their molecular mass observed after alkaline phosphatase treatment. Therefore,

%%%tau%%% 64 and 69 are specific markers of the neurofibrillary degeneration of the %%%Alzheimer%%% type and might be useful tools for studying the first pathological events that lead to neuronal death.

8/7/222 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE
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03944470 EMBASE No: 1989113463
Aluminum-induced neurofibrillary degeneration affecfts a subset of neurons in rabbit cerebral cortex, basal forebrain and upper brainstem
Kowall N.W.; Pendlebury W.W.; Kessler J.B.; Perl D.P.; Beal M.F.
Department of Neurology, Massachusetts General Hospital, Boston, MA 02114
United States
Neuroscience (NEUROSCIENCE) (United Kingdom) 1989, 29/2 (329-337)
CODEN: NRSCD ISSN: 0306-4522
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Neurofibrillary tangles in %%%Alzheimer%%%'s disease show a predilection
for cortical pyramidal and subcortical projection neurons. The antigenic composition, neuronal specificity and distribution of aluminum-induced neurofibrillary degeneration were examined in regions of rabbit brain analogous to those that develop neurofibrillary tangles in %%%Alzheimer%%%
's disease. Neurofibrillary degeneration was induced by intraventricular instillation of aluminum chloride. In aluminum-treated rabbits, intensely immunoreactive filamentous aggregates were seen in affected neuronal perikarya after staining with an anti-%%%phosphorylated%%% neurofilament
antibody (SMI 31), while in controls immunoreactivity was confined to axon-like elements. Monoclonal antibodies against Microtubule-associated protein 2 and %%%tau%%%, which stain human neurofibrillary tangles, did not
stain aluminum-induced neurofibrillary degeneration. Pyramidal neurons exhibiting neurofibrillary degeneration formed a discrete linear pattern in layers III and V of cortex. Cortical somatostatin and nicotinamide adenine dinucleotide phosphate diaphorase-reactive neurons identified in double-stained sections were unaffected. Large perikarya in the vicinity of the globus pallidus, some of which contained acetylcholinesterase, were frequently SMI 31-immunoreactive. Among the cell groups affected in the upper brainstem were the nucleus raphe dorsalis and locus coeruleus. These findings show that aluminum-induced neurofibrillary degeneration differs antigenically from neurofibrillary tangles in %%%Alzheimer%%%'s disease. Nevertheless, many neuronal subsets that are particularly suceptible to %%%Alzheimer%%%'s disease, including cortical pyramidal neurons, basal forebrain cholinergic neurons and upper brainstem catecholaminergic neurons, are also affected by aluminum-induced neurofibrillary degeneration.

8/7/223 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE
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03882293 EMBASE No: 1989051249
Immunocytochemical characterization of neurofibrillary tangles in amyotrophic lateral sclerosis and parkinsonism-dementia of Guam
Shankar S.K.; Yanagihara R.; Garruto R.M.; Grundke-Iqbal I.; Kosik K.S.; Gajdusek D.C.
Laboratory of Central Nervous System Studies, National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, MD United States
Annals of Neurology (ANN. NEUROL.) (United States) 1989, 25/2 (146-151)
CODEN: ANNED ISSN: 0364-5134
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Cryostat-cut sections of formalin-fixed and unfixed hippocampus from 23 Guamanian Chamorros with clinically and neuropathologically verified amyotrophic lateral sclerosis (ALS) (8 cases) and parkinsonism-dementia (PD) (15 cases) and from 12 neurologically normal Guamanians (5 with and 7 without neurofibrillary degeneration) were evaluated by the immunoperoxidase technique, using monoclonal antibodies against %%%phosphorylated%%% neurofilament, human fetal microtubule-associated
protein %%%tau%%%, and paired helical filaments. On immuostaining, all three antibodies showed intracellular tangles in the hippocampal neurons of patients with ALS, patients with PD, and in neurologically normal Guamanians with neurofibrillary pathology, but the correlation of immunostaining between these antibodies was not absolute. Extracellular or ghost tangles were immunostained only with the antibody against paired helical filaments. Our immunocytochemical data indicate that the antigenic composition of neurofibrillary tangles in Guamanian ALS and PD is similar to that %%%Alzheimer%%%'s disease, suggesting a common pathogenic pathway
for neurofibrillary tangle formation in these neurodegenerative disorders.

8/7/224 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE
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03862037 EMBASE No: 1989030992
Direct biochemical evidence for an abnormal %%%phosphorylation%%% of %%%Tau%%% proteins during %%%Alzheimer%%%'s disease
DEMONSTRATION DIRECTE D'UNE %%%PHOSPHORYLATION%%% ANORMALE DES PROTEINES
MICROTUBULAIRES %%%TAU%%% AU COURSE DE LA MALADIE D'%%%ALZHEIMER%%%
Flament S.; Delacourte A.; Hemon B.; Defossez A.
Unite I.N.S.E.R.M. no. 16, Laboratoire de Neurosciences, A.D.E.R.M.A., Faculte de Medecine, 59045 Lille France
Comptes Rendus de l'Academie des Sciences - Serie III (C. R. ACAD. SCI. SER. III) (France) 1989, 308/3 (77-82)
CODEN: CRASE ISSN: 0249-6313
DOCUMENT TYPE: Journal
LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH

8/7/225 (Item 16 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2002 Elsevier Science B.V. All rts. reserv.

03698760 EMBASE No: 1988148196
sup 3sup 1P nuclear magnetic resonance study of the brain in %%%Alzheimer%%%'s disease
Pettegrew J.W.; Moossy J.; Withers G.; McKeag D.; Panchalingam K.
Laboratory of Neurophysics, Department of Psychiatry and Neurology, University of Pittsburgh, Pittsburgh, PA 15213 United States
Journal of Neuropathology and Experimental Neurology (J. NEUROPATHOL.
EXP. NEUROL.) (United States) 1988, 47/3 (235-248)
CODEN: JNENA ISSN: 0022-3069
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The histopathological hallmarks of %%%Alzheimer%%%'s disease have long been considered to be neurofibrillary tangles (NFT) and neuritic (senile) plaques (SP). Neither of these structures, however, are unique to %%%Alzheimer%%%'s disease, and both probably represent end-stage markers of
the disorder. NFT have been demonstrated in many disorders; SP occur in small numbers with normal aging. Evidence is presented for elevation of phosphomonoesters (PME) in %%%Alzheimer%%%'s brain compared to non-%%%Alzheimer%%%'s diseased controls and normal controls. The PME detected
by sup 3sup 1P nuclear magnetic resonance (NMR) spectroscopy of autopsy brain are predominantly anabolic precursors of membrane phospholipids. Elevated PME could be secondary to a metabolic block at the rate-limiting enzyme in membrane phospholipid synthesis, which is cytidine triphosphate (CTP):phosphocholine (or phosphoethanolamine) cytidyltransferase (EC 2.7.7.15). Elevated PME could also be secondary to decreased breakdown of PME by phospholipase D activity. Since CTP:phosphocholine cytidyltransferase is inactivated by %%%phosphorylation%%% and since there
is independent evidence for hyperphosphorylation of %%%tau%%% and MAP-2

proteins in AD brain, enhanced protein kinase activity could be a common factor. Preliminary evidence suggests that PME could interact with N-methyl-D-aspartate receptors and potentially act as false neurotransmitters. Further studies will be needed to investigate these possibilities.

8/7/226 (Item 17 from file: 73)
DIALOG(R)File 73:EMBASE

03654623 EMBASE No: 1988104059
%%%Alzheimer%%%'s disease: Study of the distribution of Paired Helical Filaments %%%Tau%%% proteins in the human central nervous system
MALADIE D'%%%ALZHEIMER%%%: ETUDE DE LA DISTRIBUTION DES PROTEINS
%%%TAU%%% CONSTITUTIVES DES PAIRES DE FILAMENTS EN HELICE DANS LE TISSU
NERVEUX CENTRAL HUMAIN
Parent M.; Delacourte A.; Defossez A.; Hemon B.; Kia Ki Han; Petit H.
Laboratoire de Neurosciences, Faculte de Medicine de Lille, 59045 Lille Cedex France
Comptes Rendus de l'Academie des Sciences - Serie III (C. R. ACAD. SCI. SER. III) (France) 1988, 306/13 (391-397)
CODEN: CRASE ISSN: 0249-6313
DOCUMENT TYPE: Journal
LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH

%%%Tau%%% proteins are the major components of Paired Helical Filaments
(PHF) of %%%Alzheimer%%%'s disease. Using the immunoblot technique and an
antiserum against PHF, we have studied the distribution of %%%Tau%%% proteins in the different areas of normal human brains and %%%Alzheimer%%%
brains. %%%Tau%%% proteins were clearly present in cortical grey matter but
were difficult to detect in the white matter. In %%%Alzheimer%%% brains, we
observed two differences: first, there is an important background due to the partial dissociation of the lesions containing %%%Tau%%% aggregates. Second, the profile of %%%Tau%%% proteins is modified, due to abnormal %%%phosphorylation%%%. Thus, %%%Tau%%% proteins are found in large amounts
in the grey matter of the cortical areas and are not exclusively distributed in the axonal domain. The normal cortical distribution of %%%Tau%%% in the human brain correlates well with the distribution of histological lesions that contain PHF (neurofibrillary tangles and neuritic plaques) in the %%%Alzheimer%%% cortex.

8/7/227 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE

03545570 EMBASE No: 1987062506
%%%Alzheimer%%%'s paired helical filaments
Ihara Y.
Tokyo Metropolitan Institute of Gerontology, Tokyo Japan
Clinical Neurology (CLIN. NEUROL.) (Japan) 1986, 26/12 (1287-1289)
CODEN: RISHD
DOCUMENT TYPE: Journal
LANGUAGE: JAPANESE SUMMARY LANGUAGE: ENGLISH

Paired helical filaments (PHF) are unusual neuronal fibers which accumulate progressively in %%%Alzheimer%%%'s disease (AD) brain. The insolubility of PHF in various kinds of solvent enabled us to obtain highly purified PHF, but prevented application of conventional analytical methods to identify the components of PHF. Antibodies to PHF did not react with normal brain homogenates on immunoblots and stained diffuse smears on AD blots. In the course of our search for PHF precursors, we found a protein (M(r)~50 kD), strongly labeled with antiPHF in fetal brain homogenates. The characterization of the 50 kD protein showed that it was a fetal form of %%%tau%%% protein, a neuron specific microtubule-associated protein. Adult
form of %%%tau%%% protein, when partially purified, was also found to react
with antiPHF. Thus, one of the antigenic determinants of PHF is related to %%%tau%%% protein. Furthermore, antisera to PHF were found to contain a significant amount of %%%tau%%% antibodies specific for a %%%phosphorylated%%% form, but only a negligible amount of those specific
for a nonphosphorylated form. This observation suggests that a major antigenic determinant of PHF is %%%phosphorylated%%% %%%tau%%% protein.
However, we have not yet determined whether %%%phosphorylated%%% %%%tau%%%
is a major component making up the framework of the PHF fibers or a component that decorates the fibers.

8/7/228 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

03538356 EMBASE No: 1987055292
Increased in vitro %%%phosphorylation%%% of a M(r) 60,000 protein in brain from patients with %%%Alzheimer%%% disease
Saitoh T.; Dobkins K.R.
Department of Neurosciences, School of Medicine (M-024), University of California, San Diego, La Jolla, CA 92093 United States
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 1986, 83/24 (9764-9767)
CODEN: PNASA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

We have established in vitro conditions under which we can reliably measure kinase activity in normal postmortem human brain. Using these conditions, we detected in the brains of patients with %%%Alzheimer%%% disease a 2-fold increase in the level of M(r) 60,000 protein %%%phosphorylation%%% compared to age-matched controls. The M(r) 60,000
protein %%%phosphorylation%%% was found exclusively in the cytosol fraction. No differences were detected between phosphoproteins in 100,000 x
g pellet fractions from brains of %%%Alzheimer%%% disease patients and from
age-matched controls. Postmortem time up to 17 hr does not seem to affect the %%%phosphorylation%%% level of the M(r) 60,000 protein. Younger %%%Alzheimer%%% disease patients had more prominent changes in the elevation of the M(r) 60,000 protein %%%phosphorylation%%% level than older
patients, although in the control patient, age did not affect the %%%phosphorylation%%% level of the M(r) 60,000 protein. We conclude that in
the brain cytosol of %%%Alzheimer%%% disease there may be an abnormality in
either the degree of M(r) 60,000 protein %%%phosphorylation%%% or in the
M(r) 60,000 protein concentration.

8/7/229 (Item 20 from file: 73)
DIALOG(R)File 73:EMBASE

03131993 EMBASE No: 1986199570
Abnormal %%%phosphorylation%%% of the microtubule-associated protein %%%tau%%% (%%%tau%%%) in %%%Alzheimer%%% cytoskeletal pathology
Grundke-Iqbal I.; Iqbal K.; Tung Y.-C.; et al.
New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY 10314 United States
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 1986, 83/13 (44913-4917)
CODEN: PNASA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

A monoclonal antibody to the microtubule-associated protein %%%tau%%%

(
%%%tau%%%) labeled some neurofibrillary tangles and plaque neurites, the two major locations of paired-helical filaments (PHF), in %%%Alzheimer%%%
disease brain. The antibody also labeled isolated PHF that had been repeatedly washed with NaDodSOinf 4. Dephosphorylation of the tissue sections with alkaline phosphatase prior to immunolabeling dramatically increased the number of tangles and plaques recognized by the antibody. The
plaque core amyloid was not stained in either dephosphorylated or nondephosphorylated tissue sections. On immunoblots PHF polypeptides were labeled readily only when dephosphorylated. In contrast, a commercially available monoclonal antibody to a %%%phosphorylated%%% epitope of neurofilaments that labeled the tangles and the plaque neurites in tissue did not label any PHF polypeptides on immunoblots. The PHF polypeptides, labeled with the monoclonal antibody to %%%tau%%%, electrophoresed with those polypeptides recognized by antibodies to isolated PHF. The antibody to %%%tau%%%-labeled microtubules from normal human brains assembled in
vitro but identically treated %%%Alzheimer%%% brain preparations had to be
dephosphorylated to be completely recognized by this antibody. These findings suggest that %%%tau%%% in %%%Alzheimer%%% brain is an abnormally
%%%phosphorylated%%% protein component of PHF.

8/7/230 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01843449 3633759
%%%Phosphorylation%%%-dependent epitopes of neurofilament antibodies on
%%%tau%%% protein and relationship with %%%Alzheimer%%% %%%tau%%%
Lichtenberg Kraag, B.; Mandelkow, E. M.; Biernat, J.; Steiner, B.; Schroeter, C.; Gustke, N.; Meyer, H.E.; Mandelkow, E.
Max-Planck-Unit for Struct. Mol. Biol., c/o DESY, Notkestr. 85, D-2000 Hamburg 52, FRG
PROC. NATL. ACAD. SCI. USA vol. 89, no. 12, pp. 5384-5388 (%%%1992%%%)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Immunology Abstracts; CSA Neurosciences Abstracts

We have studied the %%%phosphorylation%%% of %%%tau%%% protein from
%%%Alzheimer%%% paired helical filaments, of %%%tau%%% from normal human
brain, and of recombinant %%%tau%%% isoforms. As a tool we used monoclonal
antibodies against neurofilament protein that crossreact with %%%tau%%% in
a %%%phosphorylation%%%-dependent manner. This allowed us to deduce the
state of %%%phosphorylation%%% in normal and pathological %%%tau%%%, as
well as antibody epitopes. The results suggest a role for the
%%%phosphorylation%%% sites in %%%Alzheimer%%% disease, as well as the
involvement of a Ser-Pro-directed protein kinase.

8/7/231 (Item 2 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01819917 3600945
A serine arrow right proline change in the %%%Alzheimer%%%'s disease-associated epitope %%%Tau%%% 2 results in altered secondary structure, but %%%phosphorylation%%% overcomes the conformational gap
Lang, E.; Otvos, L.,Jr.
Wistar Inst. Anat. and Biol., 3601 Spruce St., Philadelphia, PA 19104, USA
BIOCHEM. BIOPHYS. RES. COMMUN. vol. 188, no. 1, pp. 162-169 (%%%1992%%%)
ISSN: 0006-291X
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: CSA Neurosciences Abstracts

Monoclonal antibody %%%Tau%%% 2 was raised against bovine %%%tau%%%
protein, was reported to recognize a conformational epitope, and stained %%%tau%%% was found in neurofibrillary tangles of %%%Alzheimer%%%'s disease, but not normal human %%%tau%%% . We synthesized tetradeka peptides corresponding to the original bovine sequence, its serine arrow right proline substituted analog, the genuine human sequence of this region, and the bovine epitope %%%phosphorylated%%% on the crucial serine.
The secondary structure of the peptides was determined by circular dichroism. It was found that only the original bovine epitope showed a tendency to form the beta -pleated sheets characteristic of the neurofibrillary tangles. The spectra of the human peptide, its analog, and the %%%phosphorylated%%% bovine sequence were very similar, featuring a weak, helical beta -turn character.

8/7/232 (Item 3 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01800055 3574825
P42 map kinase %%%phosphorylation%%% sites in microtubule-associated protein %%%tau%%% are dephosphorylated by protein phosphatase 2A: Implications for %%%Alzheimer%%%'s disease
Goedert, M.; Cohen, E.S.; Jakes, R.; Cohen, P.
MRC Lab. Mol. Biol., Hills Rd., Cambridge, CB2 2QH, UK
FEBS LETT. vol. 312, no. 1, pp. 95-99 (%%%1992%%%)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: CSA Neurosciences Abstracts

The paired helical filament (PHF), which comprises the major fibrous element of the neurofibrillary tangle of %%%Alzheimer%%%'s disease, is composed of abnormally %%%phosphorylated%%% microtubule-associated protein
%%%tau%%%. Here we show that p42 MAP kinase %%%phosphorylates%%% recombinant %%%tau%%% and converts it to a form which is similar to PHF %%%tau%%%. Of the major serine/threonine protein phosphatases found in mammalian tissues only protein phosphatase 2A (PP2A) could dephosphorylate
%%%tau%%% %%%phosphorylated%%% in this manner, with PP2A, being the most
effective form of the enzyme.

8/7/233 (Item 4 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01669070 2907081
Phosphate analysis and dephosphorylation of modified %%%tau%%% associated
with paired helical filaments.
Ksiezak Reding, H.; Liu, Wan Kyng; Yen, Shu Hui
Dep. Pathol., Rm. 538, Albert Einstein Coll. Med., 1300 Morris Park Ave., Bronx, NY 10461, USA
BRAIN RES. vol. 597, no. 2, pp. 209-219 (%%%1992.%%%)
ISSN: 0006-8993
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Neurosciences Abstracts

We performed phosphate analysis of %%%tau%%% proteins isolated from normal human brain, %%%tau%%% proteins associated with paired helical filaments (PHF-%%%tau%%%), and %%%Alzheimer%%% %%%tau%%% not associated
with PHF. These %%%tau%%% fractions were of high purity. Normal and %%%Alzheimer%%% %%%tau%%% were purified by heat treatment, acid extraction
and calmodulin-affinity chromatography with or without HPLC. Fractions containing primarily PHF-%%%tau%%% polypeptides of 60, 64 and 68 kDa and
their degraded fragments were purified either on a sucrose density gradient

as filaments (PHF) or by heat treatment and acid extraction as amorphous proteins (PHF-%%%tau%%%). The shift in mobility was not observed with the
C-terminal fragments of 25-26 kDa, which retained the epitope to %%%Tau%%%
46. The results suggest that the %%%phosphorylation%%% sites not affected
by phosphatase may be located in the 25-26 kDa C-terminal region of PHF-%%%tau%%% and may play a role in structural stability of PHF.

8/7/234 (Item 5 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01641025 2854369
The disordered neuronal cytoskeleton in %%%Alzheimer%%%'s disease.
Lee, V.M. Y.; Trojanowski, J.Q.
Univ. Pennsylvania Sch. Med., Philadelphia, PA, USA
CURR. OPIN. NEUROBIOL. vol. 2, no. 5, pp. 653-656 (%%%1992.%%%)
DOCUMENT TYPE: Journal article; Review article LANGUAGE: ENGLISH
SUBFILE: Neurosciences Abstracts; Biochemistry Abstracts Part 3: Amino Acids, Peptides and Proteins

Evidence continues to accrue in support of the notion that normal adult human %%%tau%%% is converted into the protein subunits of %%%Alzheimer%%%'s
disease paired helical filaments as a result of the abnormal %%%phosphorylation%%% of %%%tau%%% at aberrant sizes. Although the biological consequences of the generation of these abnormal %%%tau%%% derivatives in neurons remain uncertain, it is plausible that this process could destabilize microtubules and have a deleterious effect on the function and survival of neurons. Recent studies that probe the mechanisms whereby normal %%%tau%%%, a component of the neuronal cytoskeleton, undergoes profound alterations to become paired helical filaments in the %%%Alzheimer%%%'s diseased brain are discussed.

8/7/235 (Item 6 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01639833 2852420
%%%Phosphorylation%%% of %%%tau%%% protein by purified p34 super(cdc28) and
a related protein kinase from neurofilaments.
Mawal Dewan, M.; Sen, P.C.; Abdel Ghany, M.; Shalloway, D.; Racker, E.
Sect. Biochem., Mol. and Cell Biol., Cornell Univ., Ithaca, NY 14853, USA
J. BIOL. CHEM. vol. 267, no. 27, pp. 19705-709 (%%%1992.%%%)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Biochemistry Abstracts Part 3: Amino Acids, Peptides and Proteins;
Microbiology Abstracts Section C: Algology, Mycology and Protozoology; Neurosciences Abstracts

We describe a new method for large-scale purification of p34 super(cdc28) kinase from Saccharomyces cerevisiae and show that the purified enzyme can %%%phosphorylate%%% bovine and human %%%tau%%%.
%%%Phosphorylation%%% was greatly enhanced by the addition of basic and acidic substrate modulators. The effect of the substrate modulators differed both with the structures of the substrates and the modulators. Similar results were obtained with a kinase that could be purified from neurofilaments by p13 super(suc1) affinity chromatography, a hallmark of p34 super(cdc2/cdc28)-type kinases. The results are consistent with the hypothesis that a kinase of this type is involved in %%%tau%%% %%%phosphorylation%%% in vivo and open the possibility that hyperphosphorylation in %%%Alzheimer%%%'s disease may be controlled by substrate modulators.

8/7/236 (Item 7 from file: 76)
DIALOG(R)File 76:Life Sciences Collection
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01545110 2653484
Hydrofluoric acid-treated %%%tau%%% sub(PHF) proteins display the same
biochemical properties as normal %%%tau%%% .
Greenberg, S.G.; Davies, P.; Schein, J.D.; Binder, L.I.
Dementia Res., W.M. Burke Med. Res. Inst., 785 Mamaroneck Ave., White Plains, NY 10605, USA
J. BIOL. CHEM. vol. 267, no. 1, pp. 564-569 (%%%1992.%%%)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Biochemistry Abstracts Part 3: Amino Acids, Peptides and Proteins;
Neurosciences Abstracts

%%%Tau%%% (%%%tau%%%) is a major constituent of paired helical filaments (PHF) found in %%%Alzheimer%%%'s disease. The current study examines the possibility that the distinct properties of PHF-associated %%%tau%%% proteins (%%%tau%%% sub(PHF)) result from post-translational
modifications of normal soluble %%%tau%%% (%%%tau%%% sub(s)). %%%Phosphorylation%%% of normal %%%tau%%% sub(s) appears to be responsible for the distinct properties of %%%tau%%% sub(PHF).

8/7/237 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01734301 JICST ACCESSION NUMBER: 92A0755126 FILE SEGMENT: JICST-E
Anti-PHF monoclonal antibody M4 and C5 recognize fetal type %%%phosphorylation%%% of the %%%tau%%%.
WATANABE ATSUSHI (1); HASEGAWA SHIGETO (1); IHARA YASUO (1); ARAI TAKAO (2)
; TAKIO HIROSHI (3); SUZUKI MASAMI (4); CHITANI KOICHI (4)
(1) Univ. of Tokyo; (2) Science Univ. of Tokyo; (3) Inst. of Physical and Chemical Res.; (4)Fujitahoken'eiseidai
Shinkei Kagaku(Bulletin of the Japanese Society for Neurochemistry), %%%1992%%%, VOL.31,NO.1, PAGE.206-207, FIG.1, REF.6
JOURNAL NUMBER: Y0225AAP ISSN NO: 0037-3796
UNIVERSAL DECIMAL CLASSIFICATION: 616.8 591.18.05+591.481 576.311/.316
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Conference Proceeding
ARTICLE TYPE: Short Communication
MEDIA TYPE: Printed Publication

8/7/238 (Item 2 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01733721 JICST ACCESSION NUMBER: 92A0686697 FILE SEGMENT: JICST-E
Special issue : Dementia disease and heredity in the senility. Molecular genetics of beta 4 proteins and %%%tau%%% protein.
NAKAMURA SHIGENOBU (1)
(1) Hiroshima Univ., School of Medicine
Ronen Seishin Igaku Zasshi(Japanese Journal of Geriatric Psychiatry), %%%1992%%%, VOL.3,NO.9, PAGE.978-984, FIG.2, REF.31
JOURNAL NUMBER: L1147AAG ISSN NO: 0915-6305
UNIVERSAL DECIMAL CLASSIFICATION: 616-007-07 616.8-07 575.116
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Review article
MEDIA TYPE: Printed Publication

8/7/239 (Item 3 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01626289 JICST ACCESSION NUMBER: 92A0522921 FILE SEGMENT: JICST-E
Confocal microscopic immunocytochemistry of neuropil threads and neurofibrillary tangles in aged and %%%Alzheimer%%%'s disease brains.
IWATSUBO TAKESHI (1)

(1) Univ. of Tokyo, Faculty of Medicine, Inst. of Brain Res.
Shinkei Kenkyu no Shinpo(Advances in Neurological Sciences), %%%1992%%%,
VOL.36,NO.3, PAGE.511-523, FIG.5, TBL.2, REF.42
JOURNAL NUMBER: Z0693AAP ISSN NO: 0001-8724
UNIVERSAL DECIMAL CLASSIFICATION: 616.83/.89
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: I studied immunocytochemically the neuropil threads and neurofibrillary tangles in aged and %%%Alzheimer%%%'s disease brains using a confocal laser scanning fluorescence microscope. Some of the neuropil threads visualized by %%%tau%%% antibodies were shown to occur in small dendrites, although the majority of the threads were not continuous with dendritic branches. This may suggest that normal neuronal cytoskeletons are liable to disappear in thread-bearing neurites. Double-labelling with %%%tau%%%/ubiquitin antibodies revealed that ubiquitin-immunoreactivities were lacking at one, or more often, both ends of the %%%tau%%%-positive threads. It is reasonable to speculate that the thread ends were newly formed portions, and thus the threads grow bidirectionally in dendritic branches. A PHF monoclonal antibody C5, which recognizes a %%%phosphorylated%%% epitope in the carboxyl third of %%%tau%%%, stained both intra- and extracellular NFTs, while antibodies to N-terminus of %%%tau%%% stained only the intracellular ones. N-terminus of %%%tau%%% appears to be removed, once PHFs are exposed to extracellular environment. (author abst.)

8/7/240 (Item 4 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01612713 JICST ACCESSION NUMBER: 92A0522914 FILE SEGMENT: JICST-E
Cytoskeleton and intracellular signal transduction in the nervous system Cytoskeleton. Pathological changes of the cytoskeleton in the nervous system.
NUKINA NOBUYUKI (1)
(1) Univ. of Tokyo, Faculty of Medicine, Inst. of Brain Res.
Shinkei Kenkyu no Shinpo(Advances in Neurological Sciences), %%%1992%%%,
VOL.36,NO.3, PAGE.411-419, FIG.3, REF.37
JOURNAL NUMBER: Z0693AAP ISSN NO: 0001-8724
UNIVERSAL DECIMAL CLASSIFICATION: 591.18.05+591.48 616.83/.89
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication
ABSTRACT: Several cytoskeletal changes are observed in the neurological diseases. %%%Alzheimer%%%'s neurofibrillary tangles, one of the major pathological features of %%%Alzheimer%%%'s disease, are composed of paired helical filaments(PHF). PHF has been revealed to be composed of %%%phosphorylated%%% %%%tau%%%, one of the microtubuleassociated proteins, and ubiquitin. Ubiquitin binds with the abnormal protein, which becomes a target of ATP-dependent proteolytic system. Since ubiquitin was reported to be a component of PHF, other ubiquitinated proteins in the nervous systems have been reported. Pick body, Lewy body, Glial cytoplasmic inclusion, Rosenthal fiber and abnormal inclusions in the motor neurons of patient with amyotrophic lateral sclerosis are ubiquitinated. Pick body is also composed of %%%tau%%% protein. Lewy bodies contain epitopes of neurofilament and gelsolin which is recently reported to be a component of amyloid-Finnish type. Glial cytoplasmic inclusions are immunostained with anti-.ALPHA., .BETA. tubulin and MAP5. GCI is a specific pathological marker for multiple system atrophy. Thus it is important to isolate GCI and determine the component of GCI by the protein chemical analysis. The component of Rosenthal fiber(RF) is .ALPHA. B-crystallin and the crystallin in RF is ubiquitinated. The skein-like inclusion in motor neuron is also ubiquitinated. However its component has not been determined yet. Recently it has been reported that .BETA. protein injected in rat brain induces abnormal %%%tau%%% protein in neurons near the injected sites. The components identified in the other ubiquitinated inclusions might be also induced by specific factors or in specific environments. Thus it is necessary to identify their components. (author abst.)

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01547086 JICST ACCESSION NUMBER: 92A0430490 FILE SEGMENT: JICST-E
%%%Tau%%% protein kinase.
UCHIDA TSUNEKO (1); ISHIGURO KOICHI (1); ARIOKA MANABU (1)
(1) Mitsubishi-Kasei Inst. of Life Sciences
Seikagaku, %%%1992%%%, VOL.64,NO.5, PAGE.308-312, FIG.2, TBL.1, REF.15
JOURNAL NUMBER: G0184AAZ ISSN NO: 0037-1017 CODEN: SEIKA
UNIVERSAL DECIMAL CLASSIFICATION: 577.112.016 577.15 T
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication

8/7/242 (Item 6 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01541804 JICST ACCESSION NUMBER: 92A0298363 FILE SEGMENT: JICST-E
Molecular Biology in the Investigation of Dementia. PHF: From the Viewpoint of A68 (Abnormally %%%Phosphorylated%%% %%%Tau%%%).
ENDO RIUKO (1); MORI HIROSHI (1)
(1) Univ. of Tokyo, Faculty of Medicine, Inst. of Brain Res.
Saishin Igaku, %%%1992%%%, VOL.47,NO.4, PAGE.593-601, FIG.5, TBL.2, REF.26
JOURNAL NUMBER: Z0358AAR ISSN NO: 0370-8241 CODEN: SAIGA
UNIVERSAL DECIMAL CLASSIFICATION: 616.831/.832+.85
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication
ABSTRACT: %%%Alzheimer%%%'s disease is the most common cause of dementia in elderly people. Severity of dementia correlates with brain content of two filamentous lesions: neurofibrillary tangles and senile plaques. Neurofibrillary tangles are made up of abnormal filaments, paired helical filaments composed of %%%tau%%% containing several isoforms (Mr 40,000 to Mr 60,000) that are associated with axonal microtubules. %%%Tau%%% forms in PHF are abnormally %%%phosphorylated%%% and show characteristic retarded mobility on SDS polyacrylamide gel electrophoresis. Because of its apparent molecular weight, %%%tau%%% in PHF is referred to as A68; it has been identified as an antigen for Alz-50, a monoclonal antibody. A68 merits attention because it reveals the morphology of PHF on electron microscopy. Detailed examination for A68 may elucidate the mechanism of the pathogenesis of neurofibrillary tangles ; further, prevention of abnormal %%%phosphorylation%%% of %%%tau%%% may suggest new therapeutic approaches. (author abst.)

8/7/243 (Item 7 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01393511 JICST ACCESSION NUMBER: 91A0733801 FILE SEGMENT: JICST-E
%%%Tau%%% protein and %%%Alzheimer%%%-type dementia.
HASHIMOTO KOICHI (1); NUKINA NOBUYUKI (1)
(1) Univ. of Tokyo
Ronenki Chiho(Journal of Senile Dementia), %%%1991%%%, VOL.5,NO.1, PAGE.93-99, FIG.2, REF.23
JOURNAL NUMBER: L0487AAU ISSN NO: 0914-7691
UNIVERSAL DECIMAL CLASSIFICATION: 616.831/.832+.85

LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication

8/7/244 (Item 8 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01368283 JICST ACCESSION NUMBER: 91A0497928 FILE SEGMENT: JICST-E
Dementia : a recent advance. Recent knowledge on the basic and origin of dementia. %%%Alzheimer%%% disease and %%%tau%%% protein.
MORISHIMA MAHO (1); IHARA YASUO (1)
(1) Tokyo Metrop. Inst. of Gerontology
Clin Neurosci, %%%1991%%%, VOL.9,NO.1, PAGE.28-30, FIG.4, REF.17
JOURNAL NUMBER: X0621AAY ISSN NO: 0289-0585
UNIVERSAL DECIMAL CLASSIFICATION: 616.891/.899
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication

8/7/245 (Item 9 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01112502 JICST ACCESSION NUMBER: 90A0680599 FILE SEGMENT: JICST-E
Dementia in the elderly: Causes, prevention and management. %%%Phosphorylation%%% of %%%tau%%% protein.
UCHIDA TSUNEKO (1); ISHIGURO KOICHI (1)
(1) Mitsubishi-Kasei Inst. of Life Sciences
Nippon Ronen Igakkai Zasshi(Japanese Journal of Geriatrics), %%%1990%%%, VOL.27,NO.3, PAGE.280-286, FIG.2, TBL.1, REF.15
JOURNAL NUMBER: Z0680AAH ISSN NO: 0300-9173
UNIVERSAL DECIMAL CLASSIFICATION: 616.831/.832+.85
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Commentary
MEDIA TYPE: Printed Publication
ABSTRACT: In aged human brain and particularly in %%%Alzheimer%%%'s disease brain, paired helical filaments(PHFs) accmulate in the neuronal cell. Recently, it has been found that the highly %%%phosphorylated%%% %%%tau%%% protein, one of the microtubule-associated proteins(MAPs), is a component of PHF. The authors attempted to clarify the mechanism underlying the accumulation of PHF from the following two aspects; 1) What is the mechanism of %%%phosphorylation%%% of %%%tau%%% protein? 2) Is the highly %%%phosphorylated%%% %%%tau%%% protein capable of forming PHFs? From rat or bovine microtubule proteins we partially purified and characterized a novel protein kinase that specifically %%%phosphorylated%%% %%%tau%%% and MAP2 among many proteins in the brain extract, and which formed a PHF epitope on the %%%phosphorylated%%% human %%%tau%%%. This enzyme was one of the protein serine/ threonine kinases and was independent of known second messengers. The %%%phosphorylation%%% of %%%tau%%% by this enzyme was stimulated by tubulin under the condition of microtubule formation, suggesting that the %%%phosphorylation%%% of %%%tau%%% could occur concomitantly with microtubule formation in the brain. Since this kinase was usually bound to %%%tau%%% but not directly to tubulin, the enzyme was associated with microtubules through %%%tau%%%. From these properties related to %%%tau%%%, this kinase is designated as %%%tau%%% protein kinase. The %%%tau%%% that been %%%phosphorylated%%% with this kinase using .GAMMA.-32PIATP as a phosphate donor, was digested by endoprotinase Lys-C to produce three labeled fragments, K1, K2 and K3. These three fragments were sequenced and the %%%phosphorylation%%% sites on %%%tau%%% by this kinase were identified. The K2 fragment overlapped with the %%%tau%%%-1 site known to be one of the %%%phosphorylation%%% site in PHF. This result strengthens the possibility that %%%tau%%% protein %%%phosphorylated%%% by %%%tau%%% protein kinase is incorporated into PHF. Tubulin binding sites on %%%tau%%% were located between K1 and K3 fragments, while K2 fragment was located in the neighboring to N-terminus of K1. (abridged author abst.)

8/7/246 (Item 10 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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01103086 JICST ACCESSION NUMBER: 90A0808160 FILE SEGMENT: JICST-E
%%%Tau%%% in PHF: Fragmentation, %%%phosphorylation%%%, and aggregation.
IHARA YASUO (1); KANEMARU KAZUTOMI (1); MIURA REIKO (1); HASEGAWA MASATO (1)
(1) Tokyo Metrop. Inst. of Gerontology
Kiso Roka Kenkyu(Biomedical Gerontology), %%%1990%%%, VOL.14,NO.2, PAGE.95-96, FIG.1
JOURNAL NUMBER: Y0748AAD ISSN NO: 0912-8921
UNIVERSAL DECIMAL CLASSIFICATION: 591.18.05+591.481
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Short Communication
MEDIA TYPE: Printed Publication
ABSTRACT: %%%tau%%% in PHF(paired helical filaments) is known to have unusual properties: insolubility in harsh solvents and high degree resistance to proteases. These should be major reasons why PHF progressively accumulate in %%%Alzheimer%%%'s disease(AD) brain instead of being effectively digested. Here we summarize some protein chemical characteristics of the %%%tau%%% found in PHF. Four peptides were obtained from the PHF digest, which were located in the carboxyl third of %%%tau%%%. The most carboxyl terminal regions were not brought into solution, but the study with peptide antibodies strongly suggested that that portion is also integrated into PHF. A small amount of full-length %%%tau%%% was found to be attached to Sarkosyl PHF. It is highly sensitive to proteases in contrast to the carboxyl third of %%%tau%%% in PHF and thus may be located on the surface of tangles. Immunochemical procedures revealed that the %%%tau%%% in PHF undergoes %%%phosphorylation%%% at the carboxyl terminal region. An immunochemical approach using two kinds of anti-PHF showed that this type of %%%phosphorylationis%%% specific for neonatal or juvenile %%%tau%%%, but not be detected in adult %%%tau%%%. Further observations suggested that three fragments in the most carboxyl region are the sites for this distinct %%%phosphorylation%%%. (author abst.)

8/7/247 (Item 11 from file: 94)
DIALOG(R)File 94:JICST-EPlus
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00823565 JICST ACCESSION NUMBER: 89A0069500 FILE SEGMENT: JICST-E
Senile dementia and cytoskeletal proteins.
TOKUTAKE SATOSHI (1)
(1) Psychiatric Res. Inst. of Tokyo
Shinkei Kenkyu no Shinpo(Advances in Neurological Sciences), %%%1988%%%, VOL.32,NO.6, PAGE.997-1004, FIG.6, REF.36
JOURNAL NUMBER: Z0693AAP ISSN NO: 0001-8724

UNIVERSAL DECIMAL CLASSIFICATION: 616.831/.832+.85
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Review article
MEDIA TYPE: Printed Publication
ABSTRACT: Senile Plaques, neurofibrillary tangles and amyloid congophilic angiopathy are neuropathological features characteristic of neurodegenerative diseases which present dementia such as %%%Alzheimer%%%'s disease, Creutzfeldt-Jakob disease and Kuru disease.

In these degenerating changes, fibrous structures were observed by electron microscope. Fibers of neurofibrillary tangles have been referred to as paired helical filaments (PHF). But, observation of purified PHF by negative staining method with high power electron microscope has revealed that PHF are composed of two layers of four parallel subunits, and they twist like ribbon or tape. On the other hand, fibers of senile plaques and amyloid congophilic angiopathy are 6-7nm diameter and 200-300nm in lenggth which belong to amyloid fibers. Fine structure of amyloid fibers was revealed to be tubular with six components in a circle by freeze fracture method. Fine structures of these degenerating fibers are different from those of cytoskeletal filaments such as microtubules, neurofilaments and actin filaments. Then, the relationships between these degenerating fibers and normal cytoskeletal fiers wre investigated by comparison of biochemical and immunological properties. The insolubility of these degenerating fibers has been stumbling brock to isolation and biochemical study. But, recently, PHF and amyloid fibers were purified and solubilized by high concentration of formic acid. From SDS-PAGE (sodium dodecyl sulfate-polyacrylamide gel electrophoresis) and immunological studies (immunoblotting and immunohistochemistry) of solubilized protein of PHF, it was estimated that main components of PHF is %%%phosphorylated%%% %%%tau%%% factor of microtubule-associated proteins (MAPs). While, polypeptides with the molecular weight of 4kDa were isolated from amyloid fibers and referred to as .BETA.-protein or A 4 protein. The amino acid sequence of this polypeptide as determined and cDNA encoding the precursor of .BETA.-protein was cloned. From the nucleotide se

8/7/248 (Item 1 from file: 103)
DIALOG(R)File 103:Energy SciTec

02007034 INS-87-028703; EDB-87-134707
Title: Type II CaS /calmodulin-dependent kinase %%%phosphorylates%%% %%%tau%%% protein in the region of the mouse repeat
Author(s): Kosik, K.S.; Lee, G.; Kennedy, M.B.
Affiliation: Harvard Medical School, Boston, MA
Conference Title: 78. annual meeting of the American Society of Biological Chemists conference
Conference Location: Philadelphia, PA, USA Conference Date: 7 Jun 1987
Source: Fed. Proc., Fed. Am. Soc. Exp. Biol. (United States) v 46:6.
Coden: FEPRA
Publication Date: 1 May %%%1987%%% p 2002
Report Number(s): CONF-870644-
Language: English
Abstract: %%%Tau%%% is a phosphoprotein associated with the subset of microtubules present in the axonal domain of neurons and is a component of the %%%Alzheimer%%% neurofibrillary tangle. %%%Tau%%% protein was

purified from bovine brain by the taxol method followed by gel filtration of the heat-stable microtubule fraction

CaS /calmodulin-dependent kinase was purified from rat brain as previously described. Incubation of %%%tau%%% in the kinase-containing reaction mixture resulted in intense incorporation of TSP into the protein. Labeled %%%tau%%% protein was trypsinized and separated into discrete fragments by reverse-phase HPLC. The chromatogram contained two radioactive peaks, sequenced on a gas phase sequenator. The first peak was eluted into two tubes, with more radioactivity in the second tube. The sequence in the second tube contained 16 residues which corresponded to an identical sequence in mouse %%%tau%%% that is part of a longer stretch which repeats three times with greater than 50% homology. The highest CPM's were located on a PTH-conjugated threonine.

The first tube contained the identical amino acid sequence and a lower level of radioactivity throughout unassociated with any single amino acid. About 1/3 of the total peptide was %%%phosphorylated%%%. A second

radioactive peak contained an unidentifiable PTH-amino acid present at a level below the yield obtained for %%%tau%%%.

8/7/249 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

10523595 PASCAL No.: 93-0032846
p42 map kinase %%%phosphorylation%%% sites in microtubule-associated protein %%%tau%%% are dephosphorylated by protein phosphatase 2A SUB 1 :
implications for %%%Alzheimer%%%'s disease
GOEDERT M; COHEN E S; JAKES R; COHEN P
MRC, lab. molecular biology, Cambridge CB2 2QH, United Kingdom
Journal: FEBS letters, %%%1992%%%, 312 (1) 95-99
ISSN: 0014-5793 CODEN: FEBLAL Availability: INIST-13934; 354000032074130220
No. of Refs.: 40 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: Netherlands
Language: English
The paired helical filament (PHF), which comprises the major fibrous element of the neurofibrillary tangle of %%%Alzheimer%%%'s disease, of
abnomally %%%phosphorylated%%% microtubule-associated protein %%%tau%%%.
Here we show that p42 MAP kinase %%%phosphorylates%%% recombinant %%%tau%%%
and converts it to a form which is similar to PHF %%%tau%%%. Of the major
serine/threonine protein phosphatases found in mammalian tissues only protein phosphatase 2A (PP2A) could dephosphorylate %%%tau%%%
%%%phosphorylated%%% in this manner, with PP2A, being the most effective
form of the enzyme

8/7/250 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

10520796 PASCAL No.: 93-0030047
%%%Phosphorylation%%% of %%%tau%%% protein by purified p34 SUP c SUP d
SUP c SUP 2 SUP 8 and a related protein kinase from neurofilaments
MADHUMALTI MAWAL-DEWAN; SEN P C; MOSSAAD ABDEL-GHANY; SHALLOWAY D; RACKER
E
Cornell univ., sect. biochemistry molecular cell biology, Ithaca NY 14853, USA
Journal: (The) Journal of biological chemistry, %%%1992%%%, 267 (27) 19705-19709
ISSN: 0021-9258 CODEN: JBCHA3 Availability: INIST-3082; 354000031594081020
No. of Refs.: 48 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English
It has been suggested that hyperphosphorylation of the %%%tau%%% protein
in neurofibrillary tangles may be relevant to the etiology of %%%Alzheimer%%% 's disease and that at least one of the hyperphosphorylated
sites lies within a consensus sequence for the p34 SUP c SUP d SUP c SUP 2
SUP / SUP c SUP d SUP c SUP 2 SUP 8 family of kinases. We describe a new
method for large-scale purification of p34 SUP c SUP d SUP c SUP 2 SUP 8
kinase from Saccharomyces cerevisiae and show that the purified enzyme can
%%%phosphorylate%%% bovine and human %%%tau%%%.

%%%Phosphorylation%%% was
greatly enhanced by the addition of basic and acidic substrate modulators

8/7/251 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal
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10511919 PASCAL No.: 93-0021170
A serine rightarrow proline change in the %%%Alzheimer%%%'s
disease-associated epitope %%%Tau%%% 2 results in altered secondary
structure, but %%%phosphorylation%%% overcomes the conformational gap
LANG E; OTVOS L JR
Wistar inst. anatomy biology, Philadelphia PA 19104, USA
Journal: Biochemical and biophysical research communications,
%%%1992%%%
, 188 (1) 162-169
ISSN: 0006-291X CODEN: BBRCA9 Availability: INIST-8252;
354000032123140240
No. of Refs.: 40 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English
Monoclonal antibody %%%Tau%%% 2 was raised against bovine
%%%tau%%%
protein, was reported to recognize a conformational epitope, and stained
%%%tau%%% was found in neurofibrillary tangles of
%%%Alzheimer%%%'s
disease, but not normal human %%%tau%%% . We synthesized
tetradeka
peptides corresponding to the original bovine sequence, its serine
rightarrow proline substituted analog, the genuine human sequence of this
region, and the bovine epitope %%%phosphorylated%%% on the crucial
serine.
The secondary structure of the peptides was determined by circular
dichroism

8/7/252 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal
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10447395 PASCAL No.: 92-0650878
Immunological and conformational characterization of a
%%%phosphorylated%%% immunodominant epitope on the paired helical
filaments
found in %%%Alzheimers%%%'s disease
LANG E; SZENDREI G I; LEE V M Y; OTVOS L JR
Wistar inst. anatomy biology, Philadelphia PA 19104, USA
Journal: Biochemical and biophysical research communications,
%%%1992%%%
, 187 (2) 783-790
ISSN: 0006-291X CODEN: BBRCA9 Availability: INIST-8252;
354000031587310340
No. of Refs.: 28 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English
The immunological recognition pattern of one of the most commonly used
monoclonal antibodies, PHF-1, which detects the paired helical filaments of
%%%Alzheimer%%% 's disease, exhibits a high degree of similanty with
the
recognition of a polyclonal antibody, anti-T3P, raised against a synthetic
phosphopeptide, GAEIVYKS(Phospho)PVVSGD, corresponding to amino
acids
389-402 of the microtubule-associated protein %%%tau%%% . A panel of
16
synthetic non-%%%phosphorylated%%% and %%%phosphorylated%%%
peptides,
excised from different regions of %%%tau%%% and eptide analogs
thereof,
were used to show that PHF-1 is indeed directed against the T3 fragment

8/7/253 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal
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10001615 PASCAL No.: 92-0223901
Hydrofluoric acid-treated %%%tau%%% SUB P SUB H SUB F proteins
display
the same biochemical properties as normal %%%tau%%%
GREENBERG S G; DAVIES P; SCHEIN J D; BINDER L I
W. M. Burke medical res. inst., dementia res., White Plains NY 10605, USA
Journal: (The) Journal of biological chemistry, %%%1992%%%, 267 (1)
564-569
ISSN: 0021-9258 CODEN: JBCHA3 Availability: INIST-3082;
354000023142440880
No. of Refs.: 46 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English

8/7/254 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal
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09929108 PASCAL No.: 92-0138946
Reversible b-pleated sheet formation of a %%%phosphorylated%%%
synthetic
%%%tau%%% peptide
LANG E; SZENDREI G I; ELEKES I; LEE V M Y; OTVOS L JR
Wistar inst. anatomy biology, Philadelphia PA 19104, USA
Journal: Biochemical and biophysical research communications,
%%%1992%%%
, 182 (1) 63-69
ISSN: 0006-291X CODEN: BBRCA9 Availability: INIST-8252;
354000023496950100
No. of Refs.: 27 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English Summary Language: English
Serine SUP 4 SUP 1 SUP 6 of human %%%tau%%% protein is believed to
be
%%%phosphorylated%%% in %%%Alzheimer%%% neurofibrillary
tangles. We
synthesized a fragment of %%%tau%%% , consisting of amino acids
408-421 in
both non-%%%phosphorylated%%% and serine-%%%phosphorylated%%%
forms.
Circular dichroism in a trifluoroethanol-water mixture indicated a beta
-turn rightarrow beta -pleated sheet conformational transition upon
%%%phosphorylation%%% . The beta -structure formation is intermolecular
and
can be inhibited by addition of Ca SUP 2 SUP + ions or a
%%%phosphorylated%%% tripeptide, but not with its
non-%%%phosphorylated%%%
analog

8/7/255 (Item 7 from file: 144)
DIALOG(R)File 144:Pascal
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09623576 PASCAL No.: 91-0414021
A38 : a major subunit of paired helical filaments and derivatized forms
of normal %%%tau%%%
LEE V M Y; BALIN B J; OTVOS L JR; TROJANOWSKI J Q
Univ. Pennsylvania school medicine, dep. pathology, lab. medicine,
Philadelphia PA 19104, USA
Journal: Science : (Washington, DC), %%%1991%%%, 251 (4994) 675-678
ISSN: 0036-8075 CODEN: SCIEAS Availability: INIST-6040;
354000019985670170/NUM
No. of Refs.: 22 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English

8/7/256 (Item 8 from file: 144)
DIALOG(R)File 144:Pascal

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09488942 PASCAL No.: 91-0279337
Mise en evidence de proteines %%%tau%%% anormales au cours de la degenerescence neurofibrillaire de type %%%Alzheimer%%%
(Anormal %%%tau%%% species are produced during the neurofibrillary degeneration of the %%%Alzheimer%%% type)
FLAMENT Stephane; DELACOURTE Andre, dir the
Univ.: Lille 1 Degree: Th. doct. : Sci. vie
%%%1990%%%; %%%1990%%% 189 p.
Availability: INIST-T 74023
No. of Refs.: 265 ref.
Document Type: T (Thesis) ; M (Monographic)
Country of Publication: France
Language: French
La maladie d'%%%Alzheimer%%% est caracterisee par une demence liee a la
degenerescence neurofibrillaire (DNF) des cellules pyramidales du neocortex associatif et de l'hippocampe. Dans le cytoplasme de ces neurones, s'accumulent des paquets de paires de filaments en helice (PHF) constituees par l'agregation de proteines %%%tau%%% , facteur de polymerisation des
microtubules. Une %%%phosphorylation%%% anormale de ces proteines serait a
l'origine de leur incorporation dans les PHF mais cela est discute. Nous avons compare les proteines %%%tau%%% cerebrales de malades d' %%%Alzheimer%%% a celles de temoins par la technique des immuno-transferts
grace a trois immunserums: anti-%%%tau%%%, anti-PHF et anti-PHF epuise.
Nous avons decouvert dans la substance grise des regions affectees par la DNF, trois variants de proteines %%%tau%%% dont le poids moleculaire eleve
(55, 64 et 69 kilodaltons) resulte d'une %%%phosphorylation%%% anormale.
Une etude en aveugle a confirme qu'elles etaient des marqueurs fiables de la DNF. Leur presence dans deux biopsies cerebrales suggere qu'elles sont aussi des marqueurs precoces. ces trois proteines ont ete retrouvees dans le cerveau des trisomiques 21 qui presentent une DNF semblable a celle de la maladie d'%%%Alzheimer%%% (avec PHF). Par contre, dans la maladie de
Pick et la paralysie supranucleaire progressive, ou des filaments droits s'accumulent dans les neurones en degenerescence, nous avons trouve des proteines %%%tau%%% anormales differentes des pr

8/7/257 (Item 9 from file: 144)
DIALOG(R)File 144:Pascal
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09323391 PASCAL No.: 91-0113765
%%%Tau%%% in %%%Alzheimer%%% neurobibrillary tangles : N- and C-terminal
regions are differentially associated with paired helical filaments and the location of a purative abnormal %%%phosphorylation%%% site
BRION J P; HANGER D P; BRUCE M TK; COUCK A M; FLAMENT-DURAND J; ANDERTON
B H
Univ. libre Bruxelles, lab. anatomie pathologique microscopie electronique, Brussels 1070, Belgium
Journal: Biochemical journal : (London. 1984), %%%1991%%%, 273 (1) 127-133
ISSN: 0264-6021 Availability: INIST-5003; 354000018786940160/NUM; INSERM-032
No. of Refs.: p.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United Kingdom
Language: English
To investigate the extent to which whole %%%tau%%% proteins, structurally
abnormal %%%tau%%% and fragments of %%%tau%%% are incorporated into
neurofibrillary tangles in %%%Alzheimer%%%'s disease, an immunocytochemical
mapping study using a panel of antibodies to several synthetic human %%%tau%%% peptides has been performed. Neurofibrillary tangles were
immunolabelled in situ, and paired helical filaments (PHF), the principal structural component of tangles, were immunolabelled after isolation and Pronase treatment.

8/7/258 (Item 10 from file: 144)
DIALOG(R)File 144:Pascal
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07499709 PASCAL No.: 87-0001261
Defective brain microtubule assembly in %%%Alzheimer%%%'s disease
KHALID IQBAL; GRUNDKE-IQBAL I; ZAIDI T; MERZ P A; WEN G Y; SHAIKH S S;
WISNIEWSKI H M; ALAFUZOFF I; WINBLAD B
Inst. basic res. developmental disabilities, Staten Island NY 10314, USA
Journal: Lancet (The) (British edition), %%%1986%%% (8504) 421-426
ISSN: 0140-6736 Availability: CNRS-5004
No. of Refs.: 35 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United Kingdom
Language: English
Comparaison de cerveaux etudies a l'autopsie moins de 4 h apres la mort: 3 cas de maladie d'%%%Alzheimer%%%, 5 temoins. La proteine %%%Tau%%%,
associee aux microtubules, qui stimule leur assemblage a partir de la tubuline, est anormalement phosphorylee dans la maladie d'%%%Alzheimer%%%
mais non dans les autres cas. Aucun inhibiteur n'est decele, et la tubuline peut etre assemblee par d'autres agents. La %%%phosphorylation%%% anormale
de %%%tau%%% semble jouer un role important dans la maladie d' %%%Alzheimer%%%

8/7/259 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07817944 94083961 PMID: 1341572
Cellular lesions in %%%Alzheimer%%%'s disease: structural and molecular analysis]
Les lesions cellulaires de la maladie d'%%%Alzheimer%%% : analyse structurale et moleculaire.
Brion JP
Bulletin et memoires de l'Academie royale de medecine de Belgique (BELGIUM) %%%1992%%%, 147 (11-12) p481-9; discussion 490-1, ISSN
0377-8231 Journal Code: BOX
Languages: FRENCH
Document type: Journal Article
Record type: Completed
Neurofibrillary tangles and senile plaques are the characteristic neuropathological lesions of %%%Alzheimer%%% 's disease. Neurofibrillary
tangles are composed of a microtubule-associated protein, the %%%tau%%%
protein. This protein plays a role in the development of neuronal polarity and the stabilisation of microtubules. In %%%Alzheimer%%%'s disease, %%%tau%%% proteins are abnormally %%%phosphorylated%%% on several sites.
This abnormal %%%phosphorylation%%% might induce the modifications of the
microtubule network observed in affected neurones. The main component of
the senile plaque is an amyloid deposit made of a polypeptide (beta/A4 amyloid) which derives from a larger precursor. The overexpression of this precursor in experimental models or mutations of its gene leads to the development of neuropathological lesions. The relationships between cytoskeletal abnormalities and beta/A4 amyloid are further discussed.
Record Date Created: 19940124

8/7/260 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07817643 93380395 PMID: 1308732
Neurofibrillary degeneration and microtubule associated protein %%%tau%%%

Yen SH; Liu WK
Department of Pathology, Albert Einstein College of Medicine, Bronx New York.
Chinese journal of physiology (TAIWAN) %%%1992%%%, 35 (4) p357-66,
ISSN 0304-4920 Journal Code: D36
Contract/Grant No.: AG01136, AG, NIA; AG04145, AG, NIA
Erratum in Chin J Physiol 1993;36(2) 132
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
%%%Alzheimer%%% disease is characterized by neurofibrillary pathology
containing paired helical filaments (PHF). These abnormal filaments consist of a modified form of microtubule associated protein %%%tau%%%. The
modification involves %%%phosphorylation%%%. In this mini review, we summarize recent studies regarding the differences between normal %%%tau%%%
and PHF-%%%tau%%%, focusing especially on the extent and the site of %%%phosphorylation%%%. We also discuss the mechanisms possible involved in
the development of PHF. (60 Refs.)
Record Date Created: 19931012

8/7/261 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07796316 94122962 PMID: 1669718
%%%Tau%%% proteins and neurofibrillary degeneration.
Goedert M; Spillantini MG; Crowther RA
Medical Research Council Laboratory of Molecular Biology, Cambridge, U.K.
Brain pathology (SWITZERLAND) Jul %%%1991%%%, 1 (4) p279-86, ISSN
1015-6305 Journal Code: BYB
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
The paired helical filament is the major fibrous component of neurofibrillary pathology in %%%Alzheimer%%%'s disease. Over the last three
years evidence has accumulated that the microtubule-associated protein %%%tau%%% forms an important, if not the sole, constituent of the paired
helical filament. %%%Tau%%% protein in normal brain is bound to axonal microtubules by a tandem repeat region. In %%%Alzheimer%%%'s disease a
proportion of %%%tau%%% protein becomes abnormally %%%phosphorylated%%% and
is no longer associated with axonal microtubules but instead accumulates in paired helical filaments throughout affected nerve cells. The tandem repeat region contributes substantially to the structural core of the paired helical filament, around which the amino-terminal half of the molecule forms a disordered coat. (43 Refs.)
Record Date Created: 19940225

8/7/262 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07796315 94122961 PMID: 1669717
Neurofibrillary tangles, dystrophic neurites (curly fibers), and abnormal %%%phosphorylation%%% of %%%tau%%%.
Mori H; Ihara Y
Department of Neurophysiology, Tokyo Metropolitan Institute of Gerontology, Japan.
Brain pathology (SWITZERLAND) Jul %%%1991%%%, 1 (4) p273-7, ISSN
1015-6305 Journal Code: BYB
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
(51 Refs.)
Record Date Created: 19940225

8/7/263 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07771125 91173040 PMID: 1900947
Abnormal proteins in the brain in %%%Alzheimer%%%'s disease]
Kanemaru K; Ihara Y
Department of Neurophysiology, Tokyo Metropolitan Institute of Gerontology, Japan.
Tanpakushitsu kakusan koso (JAPAN) Jan %%%1991%%%, 36 (1) p2-11, ISSN 0039-9450 Journal Code: Q7D
Languages: JAPANESE
Document type: Journal Article
Record type: Completed
Record Date Created: 19910424

8/7/264 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06964089 90160211 PMID: 2137602
Towards the development of an in vivo study model of %%%Alzheimer%%%-type
neurofibrillary degeneration]
Vers la mise au point d'un modele d'etude in vitro de la degenerescence neurofibrillaire de type %%%Alzheimer%%%.
Delacourte A; Flament S; Defossez A
Unite INSERM N 16, Laboratoire de Neurosciences, Faculte de medecine,
Lille.
La Presse medicale (FRANCE) Feb 3 %%%1990%%%, 19 (4) p170-3, ISSN
0755-4982 Journal Code: PMT
Languages: FRENCH
Document type: Journal Article
Record type: Completed
Progress in the search for the cause of %%%Alzheimer%%%'s disease is
considerably hampered by the lack of animal or in vitro model. We have shown that in %%%Alzheimer%%%'s disease two pathological variants of
%%%Tau%%% proteins, called %%%Tau%%% 64 and %%%Tau%%% 69, are regularly
present in neural tissue undergoing neurofibrillary degeneration. Beside their diagnostic value, %%%Tau%%% 64 and %%%Tau%%% 69 might enable such a
model to be devised at long last. It now seems possible to investigate for biochemical disorders capable of inducing the emergence of these two %%%Tau%%% proteins in neuron cultures or among transgenic animals. The
innumerable pathogenetic tracks of %%%Alzheimer%%%'s disease (aluminium,
zinc, superoxide dismutase and free radicals, proteases and antiproteases, beta protein A4 precursor, etc.) should then be opened to exploration.
Record Date Created: 19900320

8/7/265 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06959707 90334030 PMID: 2116081
%%%Tau%%% protein: its presence and metabolism in human neuroblastoma
cells.
Sternberg H; Mesco G; Cole G; Timiras PS
University of California, Department of Physiology-Anatomy, Berkeley.
Advances in experimental medicine and biology (UNITED STATES) %%%1990%%%, 265 p283-9, ISSN 0065-2598 Journal Code: 2LU
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
(38 Refs.)

Record Date Created: 19900905

8/7/266 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06604902 88214402 PMID: 3367156
31P nuclear magnetic resonance study of the brain in %%%Alzheimer%%%'s disease.
Pettegrew JW; Moossy J; Withers G; McKeag D; Panchalingam K
Department of Psychiatry, University of Pittsburgh, PA 15213.
Journal of neuropathology and experimental neurology (UNITED STATES) May %%%1988%%%, 47 (3) p235-48, ISSN 0022-3069 Journal Code: JBR
Contract/Grant No.: 1R01AG05657-01, AG, NIA; AG03705-05, AG, NIA; AG05133-01A1, AG, NIA; +
Erratum in J Neuropathol Exp Neurol 1989 Jan;48(1) 118-9
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The histopathological hallmarks of %%%Alzheimer%%%'s disease have long been considered to be neurofibrillary tangles (NFT) and neuritic (senile) plaques (SP). Neither of these structures, however, are unique to %%%Alzheimer%%%'s disease, and both probably represent end-stage markers of the disorder. NFT have been demonstrated in many disorders; SP occur in small numbers with normal aging. Evidence is presented for elevation of phosphomonoesters (PME) in %%%Alzheimer%%%'s brain compared to non-%%%Alzheimer%%% 's diseased controls and normal controls. The PME detected by 31P nuclear magnetic resonance (NMR) spectroscopy of autopsy brain are predominantly anabolic precursors of membrane phospholipids. Elevated PME could be secondary to a metabolic block at the rate-limiting enzyme in membrane phospholipid synthesis, which is cytidine triphosphate (CTP): phosphocholine (or phosphoethanolamine) cytidyltransferase (EC 2.7.7.15). Elevated PME could also be secondary to decreased breakdown of PME by phospholipase D activity. Since CTP: phosphocholine cytidyltransferase is inactivated by %%%phosphorylation%%% and since there is independent evidence for hyperphosphorylation of %%%tau%%% and MAP-2 proteins in AD brain, enhanced protein kinase activity could be a common factor. Preliminary evidence suggests that PME could interact with N-methyl-D-aspartate receptors and potentially act as false neurotransmitters. Further studies will be needed to investigate these possibilities.
Record Date Created: 19880610

8/7/267 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05973313 90099531 PMID: 2557644
%%%Tau%%% and ubiquitin immunoreactivity at different stages of formation of %%%Alzheimer%%% neurofibrillary tangles.
Bancher C; Brunner C; Lassmann H; Budka H; Jellinger K; Seitelberger F; Grundke-Iqbal I; Iqbal K; Wisniewski HM
Neurological Institute, University of Vienna, Austria.
Progress in clinical and biological research (UNITED STATES) %%%1989%%%, 317 p837-48, ISSN 0361-7742 Journal Code: PZ5
Contract/Grant No.: AG 04220, AG, NIA; AG 05892, AG, NIA; NS 18105, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In his original 1911 publication Alois %%%Alzheimer%%% classified neurofibrillary tangles (ANT) into three morphologically defined subgroups according to their stage of maturation. The present study shows that changes in the morphological appearance of ANT during their maturation process are accompanied by changes in their antigenic profile. As shown by several immunocytochemical studies these abnormal %%%phosphorylated%%% microtubule-associated protein %%%tau%%% and of ubiquitin. In this study, immunoreactivity for the altered %%%tau%%% is not only seen in a subset of tangles but also in the cytoplasm of some nerve cells lacking ANT, which we believe to be at a stage of neuronal alteration preceding the formation of compact tangles (Stage 0 tangles). Similar numbers of Stage 0 tangles are present in the brains of age-matched non-demented individuals as in %%%Alzheimer%%% cases, but are absent in young controls lacking ANT. In extracellular "ghost tangles", the ultimate stage of neurofibrillary degeneration, immunoreactivity for %%%tau%%% is accessible to antibodies only when tissue sections are pretreated with formic acid to uncover the binding sites. In contrast to %%%tau%%% , presence/accessibility of an epitope residing on residues 50-65 of ubiquitin recognized by a monoclonal antibody raised to paired helical filaments (3-39) increases during the maturation of ANT and is most pronounced in "ghost tangles". Appearance/uncovering of the 3-39 epitope and masking of %%%tau%%% reactivity during tangle maturation may reflect degradation or conformational changes in the pathological filaments due to their aging and the final loss of their parent nerve cells.
Record Date Created: 19900131

8/7/268 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05973303 90099520 PMID: 2690119
Neuronal cytoskeleton in the biology of %%%Alzheimer%%% disease.
Grundke-Iqbal I; Iqbal K
New York State Institute for Basic Research in Developmental Disabilities, Staten Island 10314.
Progress in clinical and biological research (UNITED STATES) %%%1989%%%, 317 p745-53, ISSN 0361-7742 Journal Code: PZ5
Contract/Grant No.: AG05892, AG, NIA; NS/AG 04220, NS, NINDS; NS18105, NS, NINDS
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
In %%%Alzheimer%%% disease the neuronal cytoskeleton is severely affected with the accumulation of paired helical filaments (PHF) in selected neurons, and a defect of microtubule assembly. Although the biochemistry of PHF is not yet completely established, the microtubule associated protein %%%tau%%% has been identified as one of their components. %%%Tau%%% in PHF is abnormally %%%phosphorylated%%%. This alteration of %%%tau%%% is present at very early stages of tangles formation. These findings indicate a defect of the neuronal %%%phosphorylation%%%/dephosphorylation system in %%%Alzheimer%%% brain. It is hypothesized that abnormal %%%phosphorylation%%%, together with other modifications might stabilize %%%tau%%% and facilitate its polymerization together with some other as yet to be identified components to PHF. The microtubule assembly defect might have direct functional consequences via compromised axoplasmic flow and neurotransmission. (38 Refs.)
Record Date Created: 19900131

8/7/269 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05949291 88310474 PMID: 3136867
%%%Alzheimer%%%'s disease: study of the distribution of %%%tau%%%
proteins constituting helical filament pairs in human central nervous tissue]
Maladie d'%%%Alzheimer%%%: Etude de la distribution des proteines %%%tau%%% constitutives des paires de filaments en helice dans le tissu nerveux central humain.
Parent M; Delacourte A; Defossez A; Hemon B; Han KK; Petit H
Laboratoire de Neurosciences, I.N.S.E.R.M. U n. 16, A.D.E.R.M., Faculte de Medecine de Lille.
Comptes rendus de l'Academie des sciences (FRANCE) %%%1988%%%, 306
(13) p391-7, ISSN 0764-4469 Journal Code: CA1
Languages: FRENCH
Document type: Journal Article
Record type: Completed
%%%Tau%%% proteins are the major components of Paired Helical Filaments
(PHF) of %%%Alzheimer%%%'s disease. Using the immunoblot technique and an
antiserum against PHF, we have studied the distribution of %%%Tau%%%
proteins in the different areas of normal human brains and %%%Alzheimer%%%
brains. %%%Tau%%% proteins were clearly present in cortical grey matter
but were difficult to detect in the white matter. In %%%Alzheimer%%%
brains, we observed two differences: first, there is an important background due to the partial dissociation of the lesions containing %%%Tau%%% aggregates. Second, the profile of %%%Tau%%% proteins is
modified, due to abnormal %%%phosphorylation%%%. Thus, %%%Tau%%% proteins
are found in large amounts in the grey matter of the cortical areas and are not exclusively distributed in the axonal domain. The normal cortical distribution of %%%Tau%%% in the human brain correlates well with the distribution of histological lesions that contain PHF (neurofibrillary tangles and neuritic plaques) in the %%%Alzheimer%%% cortex.
Record Date Created: 19880930

8/7/270 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05946885 89150983 PMID: 2493316
Direct demonstration of abnormal %%%phosphorylation%%% of %%%Tau%%%
microtubular proteins in %%%Alzheimer%%%'s disease]
Demonstration directe d'une %%%phosphorylation%%% anormale des proteines
microtubulaires %%%Tau%%% au cours de la maladie d'%%%Alzheimer%%%.
Flament S; Delacourte A; Hemon B; Defossez A
I.N.S.E.R.M. n. 16, Laboratoire de Neurosciences, Lille.
Comptes rendus de l'Academie des sciences (FRANCE) %%%1989%%%, 308
(3) p77-82, ISSN 0764-4469 Journal Code: CA1
Languages: FRENCH
Document type: Journal Article
Record type: Completed
Two polyclonal antibodies, the first raised against %%%Alzheimer%%%'s disease PHF and the second raised against human native %%%Tau%%% proteins,
led us to find two %%%Tau%%% proteins with an abnormal molecular weight of
64 and 69 kDa in %%%Alzheimer%%% brain cortices. %%%Tau%%% 64 and %%%Tau%%%
69 were never detected in control brains. The molecular weight of %%%Tau%%% 64 and 69 dramatically decreased after dephosphorylation by the
alkaline phosphatase, showing that they are abnormally %%%phosphorylated%%%
. This is the first report demonstrating their specific presence in brain regions having the %%%Alzheimer%%% pathology. They could be a very useful
tool for the study of the early events that lead to neuronal death.
Record Date Created: 19890411

8/7/271 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05932067 88312014 PMID: 2970373
Pathogenesis of amyloid formation in %%%Alzheimer%%%'s disease, Down's
syndrome and scrapie.
Wisniewski HM; Wrzolek M
New York State Office of Mental Retardation and Developmental Disabilities, Institute for Basic Research in Developmental Disabilities, Staten Island 10314.
Ciba Foundation symposium (NETHERLANDS) %%%1988%%%, 135 p224-38,
ISSN 0300-5208 Journal Code: D7X
Contract/Grant No.: AGO-4220, AG, NIA
Languages: ENGLISH
Document type: Journal Article; Review; Review, Tutorial
Record type: Completed
Paired helical filaments (PHF) are abnormal fibrous structures found in human nerve cells and their processes. Ultrastructural studies of the proto-filaments that make up the PHF revealed that the individual proto-filaments have a different substructure from normal neurofilaments or
any other known fibrous profiles. Studies using immunological and biochemical methods suggested that abnormally %%%phosphorylated%%%
%%%tau%%%, ubiquitin and neurofilament peptides are part of the PHF. Deposits of amyloid fibres in %%%Alzheimer%%%'s disease and senile dementia
of the %%%Alzheimer%%% type (AD/SDAT) are found in meningeal and brain
vessels, choroid plexus and neuritic plaques. In 1984 Glenner and Wong reported the sequence of a beta-protein isolated from cerebrovascular amyloid. We used the amino acid sequence of the cerebrovascular amyloid protein to synthesize oligonucleotide probes specific for the gene encoding this amyloid protein. Screening of a human brain cDNA library allowed us to isolate a clone which encodes the amyloid peptide. In situ hybridization studies and Southern blot analysis of a DNA sample isolated from a human-mouse hybrid cell line indicated that the corresponding genomic sequences of this cDNA clone are located on human chromosome 21. Using immunochemical and histochemical methods, we have identified the cells associated with the formation of the amyloid fibres. With immunochemical and biochemical methods we and others also showed that the protein constituting amyloid in AD/SDAT is different from amyloid in unconventional slow virus diseases. (53 Refs.)
Record Date Created: 19880927

8/7/272 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

118078577 CA: 118(9)78577t JOURNAL
p42 MAP kinase phosphorylation sites in microtubule-associated protein tau are dephosphorylated by protein phosphatase 2A1. Implications for Alzheimer's disease. (Erratum to document cited in CA118(3):20365f)
AUTHOR(S): Goedert, Michel; Cohen, E. Suzanne; Jakes, Ross; Cohen, Philip
LOCATION: Lab. Mol. Biol., MRC, Cambridge, UK, CB2 2QH
JOURNAL: FEBS Lett. DATE: 1992 VOLUME: 313 NUMBER: 2 PAGES: 203
CODEN: FEBLAL ISSN: 0014-5793 LANGUAGE: English
SECTION:
CA214010 Mammalian Pathological Biochemistry
IDENTIFIERS: erratum Alzheimer tau protein phosphorylation kinase, phosphorylation p42 kinase tau protein erratum, protein phosphatase dephosphorylation tau Alzheimer erratum
DESCRIPTORS:
Mental disorder,Alzheimer's disease...
microtubule-assocd. phosphorylated tau protein dephosphorylation by protein phosphatase 2A1 in relation to (Erratum)
Tau factors...
microtubule-assocd., p42 MAP kinase phosphorylation of, protein

phosphatase 2A1 dephosphorylation of, Alzheimer's disease in relation to (Erratum)
Phosphorylation,biological...
of microtubule-assocd. tau protein, by p42 MAP kinase, dephosphorylation of, by protein phosphatase 2A1, Alzheimer's disease in relation to (Erratum)
Dephosphorylation,biological...
of phosphorylated microtubule-assocd. tau protein, by protein phosphatase 2A1, Alzheimer's disease in relation to (Erratum)
CAS REGISTRY NUMBERS:
9025-75-6 dephosphorylation of phosphorylated microtubule-assocd. tau protein by, Alzheimer's disease in relation to (Erratum)
142243-02-5 phosphorylation of microtubule-assocd. tau protein by, dephosphorylation of, by protein phosphatase 2A1, Alzheimer's disease in relation to (Erratum)

8/7/273 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

117231502 CA: 117(23)231502r CONFERENCE PROCEEDING
Identification of an abnormal phosphorylation site in Alzheimer's disease paired helical filaments using synthetic peptides
AUTHOR(S): Lee, Virginia M. Y.; Otvos, Laszlo, Jr.
LOCATION: Sch. Med., Univ. Pennsylvania, Philadelphia, PA, 19104, USA
JOURNAL: Pept.: Chem. Biol., Proc. Am. Pept. Symp., 12th EDITOR: Smith, John A. (Ed), Rivier, Jean E (Ed), DATE: 1992 PAGES: 109-12 CODEN: 57XGA9 LANGUAGE: English MEETING DATE: 910000 PUBLISHER: ESCOM,Leiden,
Neth
SECTION:
CA214010 Mammalian Pathological Biochemistry
IDENTIFIERS: tau protein phosphorylation paired helical filament, Alzheimer disease brain tau protein phosphorylation
DESCRIPTORS:
Tau factors...
abnormal phosphorylation of, at serine residue 396, of paired helical filaments of brain, in Alzheimers disease of humans
Phosphorylation,biological...
of serine residue 396, of tau protein, of paired helical filaments of brain, in Alzheimers disease of humans
Organelle,paired helical filament...
tau protein of, abnormal phosphorylation site on, of brain, in Alzheimers disease of humans
Brain,composition...
tau protein of paired helical filaments of, abnormal phosphorylation site on, in Alzheimers disease of humans
Mental disorder,Alzheimer's disease...
tau protein of paired helical filaments of brain in, abnormal phosphorylation site on, of humans

8/7/274 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

117207740 CA: 117(21)207740w JOURNAL
Phosphorylation of Tau by purified p34cdc28 and a related protein kinase from neurofilaments
AUTHOR(S): Mawal-Dewan, Madhumalti; Sen, Parimal C.; Abdel-Ghany, Mossaad
; Shalloway, David; Racker, Efraim
LOCATION: Sect. Biochem. Mol. Cell Biol., Cornell Univ., Ithaca, NY, 14853, USA
JOURNAL: J. Biol. Chem. DATE: 1992 VOLUME: 267 NUMBER: 27 PAGES:
19705-9 CODEN: JBCHA3 ISSN: 0021-9258 LANGUAGE: English
SECTION:
CA207003 Enzymes
CA214XXX Mammalian Pathological Biochemistry
IDENTIFIERS: Tau phosphorylation neurofilament protein p34cdc28 kinase,
Alzheimer Tau phosphorylation neurofilament p34cdc28 kinase
DESCRIPTORS:
Phosphorylation,biological...
of Tau factor of human and lab animal by p34cdc28 kinase of neurofilament and yeast, substrate modulators effect on
Tau factors...
phosphorylation of, of human and lab animal by p34cdc28 kinase of yeast and neurofilament, acidic and basic substrate modulators effect on, Alzheimer's disease in relation to
Saccharomyces cerevisiae...
p34cdc28 kinase of, large-scale purifn. of
Cytoskeleton,neurofilament...
p34cdc28 kinase-like activity of, purifn. of and Tau factor of human and lab animal phosphorylation by, Alzheimer's disease in relation to
Sphingosines...
Tau factor of human and lab animal phosphorylation by p34cdc28 kinase of yeast enhancement by
Mental disorder,Alzheimer's disease...
Tau factor phosphorylation by neurofilament p34cdc28 kinase regulation by substrate modulators in relation to
CAS REGISTRY NUMBERS:
9005-49-6 reactions, Tau factor of human and lab animal phosphorylation by
p34cdc28 kinase of yeast enhancement by
143375-65-9 Tau factor of human and lab animal phosphorylation by, of neurofilament and yeast, acidic and basic substrate modulators enhancement of, Alzheimer's disease in relation to
24937-47-1 25104-18-1 25212-18-4 38000-06-5 Tau factor of human and lab
animal phosphorylation by p34cdc28 kinase of neurofilament and yeast enhancement by
9042-14-2 134195-17-8 Tau factor of human and lab animal phosphorylation
by p34cdc28 kinase of yeast enhancement by

8/7/275 (Item 4 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

117087605 CA: 117(9)87605g JOURNAL
Proteins in Alzheimer's neurofibrillary changes
AUTHOR(S): Iwatsubo, Takeshi
LOCATION: Fac. Med., Univ. Tokyo, Tokyo, Japan, 113
JOURNAL: Taisha DATE: 1992 VOLUME: 29 NUMBER: 4 PAGES: 333-42
CODEN: TSHAAW ISSN: 0372-1566 LANGUAGE: Japanese
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review Alzheimer disease tau protein phosphorylation
DESCRIPTORS:
Organelle,paired helical filament...
formation of, in Alzheimer's disease, tau protein phosphorylation in relation to, in human
Nerve,disease, neurofibrillary tangle...
in Alzheimer's disease, paired helical filament in, formation of, tau protein phosphorylation in relation to, in human
Phosphorylation,biological...
of tau protein, in Alzheimer's disease, paired helical filament formation in relation to, in human
Mental disorder,Alzheimer's disease...
paired helical filament formation in, tau protein phosphorylation in relation to, in human
Tau factors...
phosphorylation of, in Alzheimer's disease, paired helical filament formation in relation to, in human

8/7/276 (Item 5 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

117005124 CA: 117(1)5124n JOURNAL
PHF. From the viewpoint of A68 (abnormally phosphorylated tau)
AUTHOR(S): Endoh, Riuko; Mori, Hiroshi
LOCATION: Sch. Med., Univ. Tokyo, Tokyo, Japan, 113
JOURNAL: Saishin Igaku DATE: 1992 VOLUME: 47 NUMBER: 4 PAGES: 593-601
CODEN: SAIGAK ISSN: 0370-8241 LANGUAGE: Japanese

SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review paired helical filament A68 protein
DESCRIPTORS:
Organelle,paired helical filament...
phosphoprotein A68 of, in Alzheimer's disease
Mental disorder,Alzheimer's disease...
phosphoprotein A68 of paired helical filaments in
Tau factors...
68, (68,000-mol.-wt.), abnormal phosphorylation of, in paired helical filaments of brain in Alzheimer's disease

8/7/277 (Item 6 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

116004400 CA: 116(1)4400s JOURNAL
Tau in neurofibrillary tangle
AUTHOR(S): Hasegawa, Masato; Ihara, Yasuo
LOCATION: Fac. Med., Univ. Tokyo, Tokyo, Japan, 113
JOURNAL: Igaku no Ayumi DATE: 1991 VOLUME: 158 NUMBER: 9 PAGES:
511-14 CODEN: IGAYAY ISSN: 0039-2359 LANGUAGE: Japanese
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review Alzheimer disease tau protein phosphorylation, neurofibrillary tangle tau protein phosphorylation review
DESCRIPTORS:
Proteins,specific or class, A68 (Alzheimer's disease, 68,000-mol.-wt.)...
formation of, by modification of tau protein, in paired helical filaments in neurofibrillary tangles of brain, in Alzheimer's disease, in humans
Tau factors...
of paired helical filaments in neurofibrillary tangles of brain, in Alzheimer's disease, abnormal phosphorylation of, in humans
Phosphorylation,biological...
of tau protein, of paired helical filaments in neurofibrillary tangles of brain, in Alzheimer's disease, in humans
Mental disorder,Alzheimer's disease...
tau protein of paired helical filaments in neurofibrillary tangles of brain in, phosphorylation of, in humans
Organelle,paired helical filament...
tau protein of, phosphorylation of, in neurofibrillary tangles, of brain, in Alzheimer's disease, of humans

8/7/278 (Item 7 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

115205003 CA: 115(19)205003t JOURNAL
Identification and characterization of modified forms of tau in brains with Alzheimer's disease
AUTHOR(S): Yen, Shu Hui; Liu, Wan-Kyng; Ksiezak-Reding, Hanna
LOCATION: Dep. Pathol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA
JOURNAL: Adv. Behav. Biol. DATE: 1990 VOLUME: 38A NUMBER: Basic, Clin., Ther. Aspects Alzheimer's Parkinson's Dis., Vol. 1 PAGES: 169-72
CODEN: ADBBBW ISSN: 0099-6246 LANGUAGE: English
SECTION:
CA214010 Mammalian Pathological Biochemistry
IDENTIFIERS: tau protein phosphorylation brain Alzheimer disease
DESCRIPTORS:
Phosphorylation,biological...
of tau protein, of brain of humans with Alzheimer's disease
Tau factors...
phosphorylation of, of brain of humans with Alzheimer's disease
Mental disorder,Alzheimer's disease...
tau protein of brains of humans with, phosphorylation of
Brain,composition...
tau protein of, of humans with Alzheimer's disease, phosphorylation of

8/7/279 (Item 8 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

115204564 CA: 115(19)204564q JOURNAL
Phosphorylation of tau protein with a novel tau protein kinase forming paired helical filament epitopes on tau
AUTHOR(S): Ishiguro, Koichi; Sato, Kazuki; Omori, Akira; Tomizawa, Kayoko
; Uchida, Tsuneko; Imahori, Kazutomo
LOCATION: Mitsubishi Kasei Inst. Life Sci., Machida, Japan, 194
JOURNAL: Adv. Behav. Biol. DATE: 1990 VOLUME: 38A NUMBER: Basic, Clin., Ther. Aspects Alzheimer's Parkinson's Dis., Vol. 1 PAGES: 173-6
CODEN: ADBBBW ISSN: 0099-6246 LANGUAGE: English
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review tau protein kinase
DESCRIPTORS:
Mental disorder,Alzheimer's disease... Organelle,paired helical filament...
tau protein kinase in relation to
CAS REGISTRY NUMBERS:
111694-09-8 purifn. and characterization of

8/7/280 (Item 9 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

111212843 CA: 111(23)212843n JOURNAL
Characterization of two pathological Tau protein variants in Alzheimer brain cortexes
AUTHOR(S): Flament, Stephane; Delacourte, Andre; Hemon, Brigitte; Defossez, Andre
LOCATION: Lab. Neurosci., Fac. Med., F-59045, Lille, Fr.
JOURNAL: J. Neurol. Sci. DATE: 1989 VOLUME: 92 NUMBER: 2-3 PAGES:
133-41 CODEN: JNSCAG ISSN: 0022-510X LANGUAGE: English
SECTION:
CA214010 Mammalian Pathological Biochemistry
IDENTIFIERS: Tau protein phosphorylation brain Alzheimer disease
DESCRIPTORS:
Tau factors,64 (64,000-mol.-wt.)... Tau factors,69 (69,000-mol.-wt.)...
of brain in Alzheimer's disease in humans, phosphorylation in relation to
Phosphorylation,biological...
of Tau proteins, in brain in Alzheimer disease in humans
Brain,neurofibrillary tangle,disease or disorder...
Tau proteins assocd. with, phosphorylation of, in Alzheimer disease in humans
Brain,composition...
Tau proteins of regions of, in Alzheimer disease in humans, phosphorylation of

8/7/281 (Item 10 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

111002320 CA: 111(1)2320p JOURNAL
Aluminum-induced neurofibrillary degeneration affects a subset of neurons in rabbit cerebral cortex, basal forebrain and upper brainstem
AUTHOR(S): Kowall, N. W.; Pendlebury, W. W.; Kessler, J. B.; Perl, D. P.; Beal, M. F.
LOCATION: Dep. Neurol., Massachusetts Gen. Hosp., Boston, MA, 02114, USA
JOURNAL: Neuroscience (Oxford) DATE: 1989 VOLUME: 29 NUMBER: 2
PAGES: 329-37 CODEN: NRSCDN ISSN: 0306-4522 LANGUAGE: English
SECTION:
CA204003 Toxicology
IDENTIFIERS: aluminum neurofibrillary degeneration brain region
DESCRIPTORS:
Brain,toxic chemical and physical damage...
aluminum toxicity to, neurofibrillary degeneration in brain regions in, Alzheimer disease in relation to
Phosphoproteins,MAP 2 (microtubule-assocd. protein 2)... Tau factors...
of brain regions, aluminum toxicity of brain effect on, Alzheimer

disease in relation to
Cytoskeleton,neurofilament...
phosphorylated, of brain regions, aluminum toxicity to brain effect on, Alzheimer disease in relation to
CAS REGISTRY NUMBERS:
7429-90-5 biological studies, toxicity of, to brain, neurofibrillary degeneration in brain regions in, Alzheimer disease in relation to
9000-81-1 of neurons of brain regions, in aluminum-induced neurofibrillary degeneration, Alzheimer disease in relation to

8/7/282 (Item 11 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
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109227578 CA: 109(25)227578n JOURNAL
Phosphorylated microtubule protein in senile dementia
AUTHOR(S): Tokutake, Satoshi
LOCATION: Dep. Mol. Biol., Psychiatric Res. Inst. Tokyo, Tokyo, Japan, 156
JOURNAL: Dementia DATE: 1987 VOLUME: 1 NUMBER: 1 PAGES: 7-15
CODEN:
DEMEE3 LANGUAGE: Japanese
SECTION:
CA214000 Mammalian Pathological Biochemistry
IDENTIFIERS: review Alzheimer disease neurofibrillary tangle, senile plaque Alzheimer disease review
DESCRIPTORS:
Brain,neurofibrillary tangle,disease or disorder... Brain,senile plaque,disease or disorder... Nerve,neurofibrillary tangle,disease or disorder...
microscopic appearance and chem. compn. of, in Alzheimer's disease in humans
Mental disorder,Alzheimer's disease...
neurofibrillary tangles and senile plaques of brain in, microscopic appearance and chem. compn. of, in humans
Tau factors...
of neurofibrillary tangles, in Alzheimer's disease in humans
Cytoskeleton,neurofilament...
phosphorylated, of neurofibrillary tangles in Alzheimers disease in humans

8/7/283 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

09447401 Genuine Article#: U3101 Number of References: 0
Title: MICROTUBULE ASSOCIATED PROTEIN %%%TAU%%% - IMMUNOCHEMICAL EVIDENCE
FOR ITS %%%PHOSPHORYLATION%%% IN %%%ALZHEIMER%%% PAIRED HELICAL
FILAMENTS (PHF)
Author(s): GRUNDKEIQBAL I; IQBAL K
Corporate Source: NEW YORK STATE INST BASIC RES DEV DISABIL/STATEN
ISL//NY/10314
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, %%%1989%%%
, V48, N3, P331
Language: ENGLISH Document Type: MEETING ABSTRACT

8/7/284 (Item 2 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

09170301 Genuine Article#: R1440 Number of References: 52
Title: EPITOPES THAT SPAN THE %%%TAU%%%-MOLECULE ARE SHARED WITH PAIRED
HELICAL FILAMENTS
Author(s): KOSIK KS; ORECCHIO LD; BINDER L; TROJANOWSKI JQ; LEE VMY; LEE G
Corporate Source: BRIGHAM & WOMENS HOSP,DEPT MED,DIV NEUROL,CTR NEUROL
DIS/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT NEUROL
NEUROSCI/BOSTON//MA/02115; UNIV ALABAMA,SCH MED & DENT,DEPT CELL BIOL &
ANAT/BIRMINGHAM//AL/35294; UNIV PENN,DEPT PATHOL & LAB MED/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED/PHILADELPHIA//PA/19104
Journal: NEURON, %%%1988%%%, V1, N9, P817-825
Language: ENGLISH Document Type: ARTICLE

8/7/285 (Item 3 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08935368 Genuine Article#: P4500 Number of References: 29
Title: A MODIFIED FORM OF MICROTUBULE-ASSOCIATED %%%TAU%%%-PROTEIN IS THE
MAIN COMPONENT OF PAIRED HELICAL FILAMENTS
Author(s): NIETO A; CORREAS I; DEGARCINI EM; AVILA J
Corporate Source: UNIV AUTONOMA MADRID,CSIC,CTR BIOL MOLEC,CANTO
BLANCO/E-28049 MADRID//SPAIN/
Journal: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, %%%1988%%%, V
154, N2, P660-667
Language: ENGLISH Document Type: ARTICLE

8/7/286 (Item 4 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08877015 Genuine Article#: P0070 Number of References: 23
Title: %%%ALZHEIMERS%%%-DISEASE - A NEW EVIDENCE FOR COMMON EPITOPES
BETWEEN MICROTUBULE ASSOCIATED PROTEIN-%%%TAU%%% AND PAIRED HELICAL
FILAMENTS (PHF) - DEMONSTRATION AT THE ELECTRON-MICROSCOPE LEVEL BY A
DOUBLE IMMUNOGOLD LABELING
Author(s): DEFOSSEZ A; BEAUVILLAIN JC; DELACOURTE A; MAZZUCA M
Corporate Source: FAC MED LILLE,INSERM,U156,PL VERDUN/F-59045 LILLE//FRANCE/; FAC MED LILLE,HISTOL LAB/F-59045 LILLE//FRANCE/; FAC
MED LILLE,INSERM,U16/F-59045 LILLE//FRANCE/
Journal: VIRCHOWS ARCHIV A-PATHOLOGICAL ANATOMY AND HISTOPATHOLOGY,
%%%1988%%%, V413, N2, P141-145
Language: ENGLISH Document Type: ARTICLE

8/7/287 (Item 5 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08836546 Genuine Article#: N7766 Number of References: 41
Title: ALZ-50, A MONOCLONAL-ANTIBODY TO %%%ALZHEIMERS%%%-DISEASE ANTIGEN,
CROSS-REACTS WITH %%%TAU%%%-PROTEINS FROM BOVINE AND NORMAL HUMAN-BRAIN
Author(s): KSIEZAKREDING H; DAVIES P; YEN SH
Corporate Source: YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT PATHOL/BRONX//NY/10461
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, %%%1988%%%, V263, N17, P7943-7947
Language: ENGLISH Document Type: ARTICLE

8/7/288 (Item 6 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08814175 Genuine Article#: N4987 Number of References: 0
Title: INTRANEURONAL ACCUMULATION OF %%%PHOSPHORYLATED%%% %%%TAU%%%
PRECEDES THE FORMATION OF %%%ALZHEIMER%%%

NEUROFIBRILLARY TANGLES (ANT)
Author(s): BANCHER C; BRUNNER C; LASSMANN H; BUDKA H; JELLINGER K;
SEITELBERGER F; GRUNDKEIQBAL I; IQBAL K; WISNIEWSKI HM
Corporate Source: VIENNA UNIV,INST NEUROL/A-1010 VIENNA//AUSTRIA/; NEW YORK
STATE INST BASIC RES DEV DISABIL/STATEN ISL//NY/10314; L BOLTZMANN INST
CLIN NEUROBIOL/VIENNA//AUSTRIA/
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, %%%1988%%%
, V47, N3, P335
Language: ENGLISH Document Type: MEETING ABSTRACT

8/7/289 (Item 7 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08738468 Genuine Article#: N0443 Number of References: 20
Title: THE MONOCLONAL-ANTIBODY, ALZ 50, RECOGNIZES %%%TAU%%%-PROTEINS IN
%%%ALZHEIMERS%%%-DISEASE BRAIN
Author(s): NUKINA N; KOSIK KS; SELKOE DJ
Corporate Source: BRIGHAM & WOMENS HOSP,CTR NEUROL DIS,DEPT MED NEUROL,75
FRANCIS ST/BOSTON//MA/02115; HARVARD UNIV,SCH MED,DEPT NEUROL
NEUROSCI/BOSTON//MA/02115
Journal: NEUROSCIENCE LETTERS, %%%1988%%%, V87, N3, P240-246
Language: ENGLISH Document Type: ARTICLE

8/7/290 (Item 8 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08472291 Genuine Article#: L0820 Number of References: 32
Title: INVITRO CONDITIONS FOR THE SELF-POLYMERIZATION OF THE
MICROTUBULE-ASSOCIATED PROTEIN, %%%TAU%%% FACTOR
Author(s): DEGARCINI EM; AVILA J
Corporate Source: UNIV AUTONOMA MADRID,CSIC,CTR BIOL MOLEC,CANTO
BLANCO/E-28049 MADRID//SPAIN/
Journal: JOURNAL OF BIOCHEMISTRY, %%%1987%%%, V102, N6, P1415-1421
Language: ENGLISH Document Type: ARTICLE

8/7/291 (Item 9 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08411416 Genuine Article#: K5706 Number of References: 53
Title: %%%TAU%%%-ANTISERA RECOGNIZE NEUROFIBRILLARY TANGLES IN A RANGE OF
NEURODEGENERATIVE DISORDERS
Author(s): JOACHIM CL; MORRIS JH; KOSIK KS; SELKOE DJ
Corporate Source: HARVARD UNIV,BRIGHAM & WOMENS HOSP,SCH MED,CTR NEUROL
DIS,75 FRANCIS ST/BOSTON//MA/02115; HARVARD UNIV,BRIGHAM & WOMENS
HOSP,SCH MED,DEPTPATHOL/BOSTON//MA/02115
Journal: ANNALS OF NEUROLOGY, %%%1987%%%, V22, N4, P514-520
Language: ENGLISH Document Type: ARTICLE

8/7/292 (Item 10 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08389134 Genuine Article#: K4223 Number of References: 34
Title: %%%TAU%%%-EPITOPES ARE INCORPORATED INTO A RANGE OF LESIONS IN
%%%ALZHEIMERS%%%-DISEASE
Author(s): JOACHIM CL; MORRIS JH; SELKOE DJ; KOSIK KS
Corporate Source: HARVARD UNIV,BRIGHAM & WOMENS HOSP,SCH MED,CTR NEUROL
DIS,75 FRANCIS ST/BOSTON//MA/02115; HARVARD UNIV,BRIGHAM & WOMENS
HOSP,SCH MED,DEPTPATHOL/BOSTON//MA/02115
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, %%%1987%%%
, V46, N6, P611-622
Language: ENGLISH Document Type: ARTICLE

8/7/293 (Item 11 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08097042 Genuine Article#: H3882 Number of References: 39
Title: RECOGNITION OF %%%TAU%%% EPITOPES BY ANTI-NEUROFILAMENT ANTIBODIES
THAT BIND TO %%%ALZHEIMER%%% NEUROFIBRILLARY TANGLES
Author(s): KSIEZAKREDING H; DICKSON DW; DAVIES P; YEN SH
Corporate Source: YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT PATHOL/BRONX//NY/10461
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED
STATES OF AMERICA, %%%1987%%%, V84, N10, P3410-3414
Language: ENGLISH Document Type: ARTICLE

8/7/294 (Item 12 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08043131 Genuine Article#: G9858 Number of References: 0
Title: %%%PHOSPHORYLATED%%% %%%TAU%%% PROTEIN IS PRESENT IN NEURONAL
CELL-BODIES AND DENDRITES OF CONTROL AND
BETA,BETA'-IMINODIPROPIONITRILE (IDPN)-TREATED RATS - IMPLICATIONS FOR
THE PATHOGENESIS OF %%%ALZHEIMERS%%%-DISEASE (AD)
Author(s): PAPASOZOMENOS SC; BINDER LI
Corporate Source: UNIV TEXAS/HOUSTON//TX/77025; UNIV ALABAMA/BIRMINGHAM//AL/35294
Journal: JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, %%%1987%%%
, V46, N3, P349
Language: ENGLISH Document Type: MEETING ABSTRACT

8/7/295 (Item 13 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

07911948 Genuine Article#: G1980 Number of References: 31
Title: HIRANO BODIES CONTAIN %%%TAU%%% PROTEIN
Author(s): GALLOWAY PG; PERRY G; KOSIK KS; GAMBETTI P
Corporate Source: CLEVELAND METROPOLITAN GEN HOSP,DEPT PATHOL,3395 SCRANTON
RD/CLEVELAND//OH/44109; CASE WESTERN RESERVE UNIV,INST PATHOL,DIV
NEUROPATHOL/CLEVELAND//OH/44106; HARVARD UNIV,SCH MED,DEPT
NEUROL/BOSTON//MA/02115
Journal: BRAIN RESEARCH, %%%1987%%%, V403, N2, P337-340
Language: ENGLISH Document Type: NOTE

8/7/296 (Item 14 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
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07869485 Genuine Article#: F8701 Number of References: 45
Title: %%%ALZHEIMERS%%% NEUROFIBRILLARY TANGLES CONTAIN UNIQUE EPITOPES AND
EPITOPES IN COMMON WITH THE HEAT-STABLE MICROTUBULE ASSOCIATED PROTEINS

%%%TAU%%% AND MAP2
Author(s): YEN SH; DICKSON DW; CROWE A; BUTLER M; SHELANSKI ML
Corporate Source: YESHIVA UNIV ALBERT EINSTEIN COLL MED,DEPT PATHOL
NEUROPATHOL,1300 MORRIS PK AVE,F-538/BRONX//NY/10461; NYU,SCH MED,DEPT
PHARMACOL/NEW YORK//NY/10003; ROSE F KENNEDY CTR RES MENTAL RETARDAT &
HUMAN DEV/NEW YORK//NY/00000
Journal: AMERICAN JOURNAL OF PATHOLOGY, %%%1987%%%, V126, N1, P81-91
Language: ENGLISH Document Type: ARTICLE

8/7/297 (Item 15 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

07692624 Genuine Article#: F2092 Number of References: 20
Title: SELF ASSEMBLY OF MICROTUBULE ASSOCIATED PROTEIN-%%%TAU%%% INTO
FILAMENTS RESEMBLING THOSE FOUND IN %%%ALZHEIMER%%%-DISEASE
Author(s): DEGARCINI EM; SERRANO L; AVILA J
Corporate Source: UNIV AUTONOMA MADRID,CSIC,CTR BIOL MOLEC,CANTO
BLANCO/E-28049 MADRID//SPAIN/
Journal: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, %%%1986%%%, V
141, N2, P790-796
Language: ENGLISH Document Type: ARTICLE

8/7/298 (Item 16 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

07673877 Genuine Article#: F0405 Number of References: 36
Title: %%%ALZHEIMERS%%%-DISEASE - %%%TAU%%% PROTEINS, THE PROMOTING FACTORS
OF MICROTUBULE ASSEMBLY, ARE MAJOR COMPONENTS OF PAIRED HELICAL
FILAMENTS
Author(s): DELACOURTE A; DEFOSSEZ A
Corporate Source: INSERM,UNITE 16,PL VERDUN/F-59045 LILLE//FRANCE/;
INSERM,UNITE 156/F-59045 LILLE//FRANCE/
Journal: JOURNAL OF THE NEUROLOGICAL SCIENCES, %%%1986%%%, V76, N2-3, P
173-186
Language: ENGLISH Document Type: ARTICLE

8/7/299 (Item 17 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
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07328503 Genuine Article#: C5907 Number of References: 46
Title: MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% (%%%TAU%%%) IS A MAJOR
ANTIGENIC COMPONENT OF PAIRED HELICAL FILAMENTS IN %%%ALZHEIMER%%%
-DISEASE
Author(s): KOSIK KS; JOACHIM CL; SELKOE DJ
Corporate Source: HARVARD UNIV,BRIGHAM & WOMENS HOSP,CTR NEUROL DIS,75
FRANCIS ST/BOSTON//MA/02115
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED
STATES OF AMERICA, %%%1986%%%, V83, N11, P4044-4048
Language: ENGLISH Document Type: ARTICLE

8/7/300 (Item 18 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
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07328502 Genuine Article#: C5907 Number of References: 26
Title: NEUROFIBRILLARY TANGLES OF %%%ALZHEIMER%%%-DISEASE SHARE ANTIGENIC
DETERMINANTS WITH THE AXONAL MICROTUBULE-ASSOCIATED PROTEIN %%%TAU%%% (
%%%TAU%%%)
Author(s): WOOD JG; MIRRA SS; POLLOCK NJ; BINDER LI
Corporate Source: EMORY UNIV,SCH MED,DEPT ANAT & CELL BIOL/ATLANTA//GA/30322; EMORY UNIV,SCH MED,DEPT PATHOL & LAB
MED/ATLANTA//GA/30322; UNIV ALABAMA,DEPT CELL BIOL & ANAT/BIRMINGHAM//AL/35294; VET ADM MED CTR/ATLANTA//GA/30322
Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED
STATES OF AMERICA, %%%1986%%%, V83, N11, P4040-4043
Language: ENGLISH Document Type: ARTICLE

8/7/301 (Item 19 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

07282692 Genuine Article#: C1469 Number of References: 11
Title: ONE OF THE ANTIGENIC DETERMINANTS OF PAIRED HELICAL FILAMENTS IS
RELATED TO %%%TAU%%% PROTEIN
Author(s): NUKINA N; IHARA Y
Corporate Source: UNIV TOKYO,FAC MED,INST BRAIN RES,DEPT NEUROL,BUNKYO
KU/TOKYO 113//JAPAN/; TOKYO METROPOLITAN INST GERONTOL/TOKYO
173//JAPAN/
Journal: JOURNAL OF BIOCHEMISTRY, %%%1986%%%, V99, N5, P1541-1544
Language: ENGLISH Document Type: NOTE

8/7/302 (Item 20 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
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07264763 Genuine Article#: C1710 Number of References: 35
Title: MICROTUBULE-ASSOCIATED PROTEIN-%%%TAU%%% - A COMPONENT OF
%%%ALZHEIMER%%% PAIRED HELICAL FILAMENTS
Author(s): GRUNDKEIQBAL I; IQBAL K; QUINLAN M; TUNG YC; ZAIDI MS;
WISNIEWSKI HM
Corporate Source: NEW YORK STATE OFF MENTAL RETARDAT & DEV DISABIL,INST
BASIC RES DEV DISABIL/STATEN ISL//NY/10314
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, %%%1986%%%, V261, N13, P6084-6089
Language: ENGLISH Document Type: ARTICLE
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Set Items Description
S1 15749 TAU AND ALZHEIMER?
S2 102 S1 AND PROTEIN(W)SEQUENC?
S3 74 RD S2 (unique items)
S4 19 S3 AND PY<1992
S5 10505 TAU AND PHOSPHORYLAT?
S6 1397 S5 AND PY<1993
S7 602 RD S6 (unique items)
S8 302 S7 AND ALZHEIMER?
? s s7 and epitope?

602 S7
293614 EPITOPE?
S9 95 S7 AND EPITOPE?
? s s9 not s7

95 S9
602 S7

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Set    Items   Description
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S2       102   S1 AND PROTEIN(W)SEQUENC?
S3        74   RD S2 (unique items)
S4        19   S3 AND PY<1992
S5     10505   TAU AND PHOSPHORYLAT?
S6      1397   S5 AND PY<1993
S7       602   RD S6 (unique items)
S8       302   S7 AND ALZHEIMER?
S9        95   S7 AND EPITOPE?
S10        0   S9 NOT S7
? s s9 not s8

         95  S9
        302  S8
   S11     10  S9 NOT S8
? t s11/7/all

>>>Format 7 is not valid in file 143

 11/7/1    (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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08741076   BIOSIS NO.: 199395030427
Regional distribution and biochemical characteristics of high molecular
  weight %%%tau%%% in the nervous system.
AUTHOR: Taleghany N; Oblinger Monica M(a)
AUTHOR ADDRESS: (a)Dep. Cell Biol. Anat., Chicago Med. Sch., 3333 Green
Bay
  Rd., North Chicago, Ill. 60064
JOURNAL: Journal of Neuroscience Research  33 (2):p257-265
%%%1992%%%
ISSN: 0360-4012
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The present study examined the distribution of the high
molecular
  weight (HMW) %%%tau%%% protein isoform in the nervous system by
  immunoblotting and immunohistochemistry. Some of the biochemical
  properties of this 110 kDa %%%tau%%% protein were explored, including
its
  heat stability, %%%phosphorylation%%% and partitioning with cold/Ca-2+
  stable vs. soluble microtubules. Qualitative western blot analysis
  revealed that HMW %%%tau%%% is preferentially expressed in neurons
with
  peripherally projecting axons. For example, this isotype was present in
  sciatic nerve, ventral and dorsal roots, trigeminal nerve, vagus nerve,
  dorsal root ganglia (DRG) and spinal cord, but was present in only trace
  amounts in CNS regions. Another %%%tau%%% isoform of sightly smaller
size
  (90-100 kDa), termed mid-molecular weight (MMW) %%%tau%%%, was
present in
  abundant quantity in optic nerve samples and detectable in several other
  CNS regions, including hippocampus and cerebellum. The 110 kDa HMW
  %%%tau%%% as well as MMW %%%tau%%% and the other %%%tau%%%
isoforms were
  found to be heat stable proteins. The HMW and MMW %%%tau%%%
isoforms
  preferentially partitioned with the cold and Ca+2 insoluble tubulin
  fraction, but the association of HMW %%%tau%%% with stable
microtubules
  was very susceptible to proteolysis. Dephosphorylation of fresh tissue
  with alkaline phosphatase produced no apparent shift in the mobilityof
  HMW %%%tau%%% on SDS-PAGE but did alter the mobility of other brain
  %%%tau%%% isoforms, including MMW %%%tau%%%.
Immunocytochemical staining
  with %%%tau%%%-1 antibody in the DRG, which contains HMW
%%%tau%%% but no
  other %%%tau%%% isotypes, showed localization of mainly small neurons
and
  was not altered by dephosphorylation of the histological sections. This
  suggest that HMW %%%tau%%%, which contains the %%%tau%%%-1
%%%epitope%%%,
  is not %%%phosphorylated%%% in that site.


 11/7/2    (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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08729358   BIOSIS NO.: 199395018709
Cytoskeletal immunohistochemistry of central neurocytomas.
AUTHOR: Hessler R B; Lopes M B S; Frankfurter A; Reidy J; Vandenberg S
R(a)
AUTHOR ADDRESS: (a)Dep. Pathol., Box 214, Univ. Virginia Health Sci.
Cent.,
  Charlottesville, Va. 22908
JOURNAL: American Journal of Surgical Pathology  16 (11):p1031-1038
%%%1992%%%
ISSN: 0147-5185
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Central neurocytomas are rare intraventricular tumors. Patients
  with such tumors have a favorable prognosis after surgical removal. These
  tumors may be misdiagnosed as neuroblastomas or gliomas, risking the
  complications of adjuvant therapy. Diagnosis of central neurocytoma
  requires that the tumor shows the ultrastructural features of mature
  neuronal differentiation, including the presence of synapses and
  dense-core and clear vesicles in addition to profiles of neuritic
  processes with microtubules. The cytoskeletal phenotype of central
  neurocytomas has not been previously characterized, but it may facilitate
  their definitive recognition when ultrastructural examination is not
  possible. Ten central neurocytomas were examined by
immunohistochemistry
  for %%%phosphorylation%%%-dependent/independent neurofilament
  %%%epitopes%%%, neuron-associated class III beta-tubulin,
  microtubule-associated proteins (MAP2, %%%tau%%%), and glial fibrillary
  acidic protein (GFAP). The neuronal nature of all neoplasmas was
  documented by immunoreactivity for synaptophysin in nine tumors and for
  %%%phosphorylation%%%-independent neurofilament-H/M in the
remaining
  case. Electron microscopy in four cases showed synapses and dense core
  vesicles. All tumors were immunoreactive for class III beta-tubulin and
  MAP2, which were seen in cytoskeletal structures by immunoelectron
  microscopy. Two thirds of the cases were immunohistochemically positive
  for neurofilament %%%epitopes%%%. None of the tumor cells displayed
GFAP
  immunoreactivity, although reactive astrocytes were present. These data
  suggest that central neurocytomas may be recognized by synaptophysin
  immunoreactivity and that the expression of cytoskeletal
%%%epitopes%%%
  indicates that these tumors are well-differentiated neuronal neoplasms.


 11/7/3    (Item 3 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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08092283   BIOSIS NO.: 000093102356
COMMON %%%EPITOPES%%% OF HUMAN AND MURINE MALLORY
BODIES AND LEWY BODIES AS
  REVEALED BY A NEUROFILAMENT ANTIBODY
AUTHOR: PREISEGGER K-H; ZATLOUKAL K; SPUREJ G; RIEEIGELNEGG D;
DENK H
AUTHOR ADDRESS: DIV. MOL. PATHOL., INST. PATHOL., UNIV. GRAZ
SCH. MED.,
  AUENBRUGGERPLATZ. 25, A-8036 GRAZ, AUSTRIA.
JOURNAL: LAB INVEST 66 (2). 1992. 193-199. %%%1992%%%
FULL JOURNAL NAME: Laboratory Investigation
CODEN: LAINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH
```

ABSTRACT: The antibody SMI 31, which is directed against a %%%phosphorylated%%% %%%epitope%%%, associated with neurofilaments and
recognizes Lewy bodies in brains of patients with Parkinson's disease (Bancher C, Lassmann H, Budka H. Jellinger K, Grundgke-Iqbal I, Iqbal K, Wiche G, Seitelberger F, Wisniewski H: J Neuropathol Exp Neurol 1:81, 1989), decorated in immunofluorescence microscopy Mallory bodies (MBs) present in livers of mice chronically treated with griseofulvin and 3,5-diethoxycarbonyl-1,4-dihydrocollidine. In the immunoblots it recognized very acidic MB components in a molecular weight range between 55 and 69.5 kilodaltons in addition to poorly soluble high molecular weight material. Moreover, an antibody to %%%tau%%% protein showed similar reactivities in immunofluorescence microscopy and immunoblotting experiments. Both antibodies also stained MBs in human liver with alcoholic hepatitis. These observations support and extend earlier findings which indicate that several intermediate filament-related cellular inclusion bodies, including MBs, share a variety of morphologic, structural and antigenic features. They also suggest the involvement of %%%tau%%% or %%%tau%%%-like proteins in MB formation.

11/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07618856 BIOSIS NO.: 000091136740
ALUMINUM MALTOL-INDUCED NEUROCYTOSKELETAL CHANGES IN FETAL RABBIT MIDBRAIN
IN MATRIX CULTURE
AUTHOR: HEWITT C D; HERMAN M M; LOPES M B S; SAVORY J; WILLS M R
AUTHOR ADDRESS: DEP. PATHOL., UNIV. VA. HEALTH SCI. CENT., CHARLOTTESVILLE,
VA. 22908, USA.
JOURNAL: NEUROPATHOL APPL NEUROBIOL 17 (1). 1991. 47-60. %%%1991%%%
FULL JOURNAL NAME: Neuropathology and Applied Neurobiology
CODEN: NANED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have developed a neuronal culture system to evaluate the neurotoxic effects of aluminium maltol on fetal rabbit midbrain sections containing the oculomotor nucleus. Cultures were treated with 5, 7, 9, 11, 13 and 15 .mu.mol/l aluminium maltol or 39 and 45 .mu.mol/l maltol (molal equivalents to 13 and 15 .mu.mol/l aluminium maltol). Control cultures were maintained in nutrient medium alone. Silver-positive neuritic swellings and occasional perikaryal neurofibrillary tangles were observed in cultures treated with 11, 13 and 15 .mu.mol/l aluminium maltol. The number of tangles (involved neurons) produced in aluminium maltol treated cultures were counted and compared to (untreated) controls. We observed a total of 3, 7 and 7% of involved neurons following treatment with 11, 13 and 15 .mu.mol/l aluminium maltol respectively, and none in the control group. By immunohistochemistry, neurofibrillary tangles were immunoreactive with MAbs to %%%phosphorylated%%% (SMI-31), non-%%%phosphorylated%%%, %%%phosphorylation%%% dependent (SMI-32) and %%%phosphorylation%%%
independent (SMI-33) %%%epitopes%%% of the high (-H) and middle (-M) molecular weight neurofilament subunits (NF-H/M). By contrast these lesions were non-reactive with MAbs recognizing %%%tau%%%, MAP2 or different .beta.-tubulin isotypes. The perikaryal tangles consisted of focal accumulations of 10 nm straight filaments by electron microscopy. These findings are in agreement with previous data from rabbit in vivo studies after the administration of aluminium maltol intravenously (Berthelf et al., 1989) or intraventricularly (Katsetos et al., 1990). Using this in vitro system, aluminium-induced neurofibrillary tangles can be consistently produced, and changes in the distribution of neurofilament proteins evaluated. These studies may aid in the assessment of the possible role of aluminium in the etiology of human neurodegenerative disorders.

11/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06619784 BIOSIS NO.: 000087061946
AN ANTIGENIC PROFILE OF LEWY BODIES IMMUNOCYTOCHEMICAL INDICATION FOR
PROTEIN %%%PHOSPHORYLATION%%% AND UBIQUITINATION
AUTHOR: BANCHER C; LASSMANN H; BUDKA H; JELLINGER K; GRUNDKE-IQBAL I; IQBAL
K; WICHE G; SEITELBERGER F; WISNIEWSKI H M
AUTHOR ADDRESS: NEUROLOGICAL INST. UNIV. VIENNA, SCHWARZSPANIERSTRASSE 17,
1090 WIEN, AUSTRIA.
JOURNAL: J NEUROPATHOL EXP NEUROL 48 (1). 1989. 81-93. %%%1989%%%
FULL JOURNAL NAME: Journal of Neuropathology & Experimental Neurology
CODEN: JNENA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: An antigenic profile of subcortical and cortical Lewy bodies was determined in the presence or absence of neurofibrillary tangles in the same brain using antisera and monoclonal antibodies to various cytoskeletal elements as well as to determinants not present in the normal cytoskeleton. The cores of many Lewy bodies were strongly reactive with a monoclonal antibody to paried helical filaments which has been shown to recognize ubiquitin. This antibody also stained Marinesco bodies in the same tissue sections. Two monoclonal antibodies to %%%phosphorylated%%% %%%epitopes%%% of neurofilament proteins (SM I 31,
SM I 34) stained the peripheries of about 40% of all discernable Lewy bodies on untreated paraffin sections. Reactivity with a monoclonal antibody to neurofilaments (SM I 33) appeared only after pretreatment of the sections with phosphatase. Lewy bodies did not bind antibodies to %%%tau%%% protein. Our results show that, as previously shown for neurofibrillary tangles, Lewy bodies also contain ubiquitin. The uncovering of neurofilament %%%epitopes%%% by treatment with phosphatase
indicates that abnormal %%%phosphorylation%%% of cytoskeletal elements
may play a role in the pathogenesis of the Lewy body.

11/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06097134 BIOSIS NO.: 000085060283
ACCUMULATION OF %%%PHOSPHORYLATED%%% NEUROFILAMENTS IN ANTERIOR HORN
MOTONEURONS OF AMYOTROPHIC LATERAL SCLEROSIS PATIENTS
AUTHOR: MUNOZ D G; GREENE C; PERL D P; SELKOE D J
AUTHOR ADDRESS: DEP. PATHOL., COLL. MED., UNIV. SASKATCHEWAN, SASKATOON,
SASKATCHEWAN S7N 0W0, CANADA.
JOURNAL: J NEUROPATHOL EXP NEUROL 47 (1). 1988. 9-18. %%%1988%%%
FULL JOURNAL NAME: Journal of Neuropathology & Experimental Neurology
CODEN: JNENA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Perikaryal collections of intermediate filaments have been described in the anterior horn motoneurons of patients with amyotrophic lateral sclerosis (ALS), but these inclusions have generally been considered rare and mainly associated with the familial form of ALS. Using the monoclonal antibody NF2F11, which recognizes %%%phosphorylated%%% neurofilament %%%epitopes%%%, we showed that focal
collections of neurofilaments in anterior horn motoneurons were a characteristic finding in sporadic as well as in familial ALS; they were present in seven of nine ALS patients, but in none of nine control spinal cords. These neurofilamentous collections are not cross-reactive with antibodies directed against paired helical filaments anbd the microtubule associated protein %%%tau%%%. In addition, diffuse staining for %%%phosphorylated%%% neurofilament %%%epitopes%%% in chromatolytic

anterior horn perikarya was significantly more frequent in ALS patients than in controls.

11/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06086926 BIOSIS NO.: 000085050075
%%%PHOSPHORYLATION%%% DETERMINES TWO DISTINCT SPECIES OF %%%TAU%%% IN THE CENTRAL NERVOUS SYSTEM
AUTHOR: PAPASOZOMENOS S C; BINDER L I
AUTHOR ADDRESS: DEP. PATHOL., LAB. MED., UNIV. TEX. MED. SCH., PO BOX 20708, HOUSTON, TEX. 77225, USA.
JOURNAL: CELL MOTIL CYTOSKELETON 8 (3). 1987. 210-226. %%%1987%%%
FULL JOURNAL NAME: Cell Motility and the Cytoskeleton
CODEN: CMCYE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The monoclonal antibody, %%%Tau%%%-1, which had previously been used to localize %%%tau%%% to the axonal compartment in brain has been reutilized for light and electron microscopic immunohistochemistry following phosphatase treatment of tissue. We report here that a signficiant quantity of %%%tau%%% in the central nervous system is %%%phosphorylated%%% in situ at or near the %%%Tau%%%-1 %%%epitope%%%, preventing the binding of the %%%Tau%%%-1 antibody. Upon removal of this/these phosphate group(s), however, %%%Tau%%%-1 was observed in the somatodendritic compartment of neurons as well as in axons. Furthermore, intense staining was also observed in astrocytes and in perineuronal glial cells. This immunoreactivity was present along the lengths of microtubules and on ribosomes (polysomes). Treatment of immunoblots of extracts of whole cerebral cortex with phosphatase confirmed the immunohistochemical results in that a 50-65% increase in %%%Tau%%%-1 binding to the %%%tau%%% region of the blot was noted. Moreover, a novel monoclonal antibody, %%%Tau%%%-2, was also used in these experiments. This antibody binds only to %%%tau%%% and localizes along microtubules in axons, somata, dendrites, and astrocytes and on ribosomes (polysomes) without phosphatase pretreatment.

11/7/8 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01712492 Genuine Article#: HV090 Number of References: 40
Title: THE JUVENILE MICROTUBULE-ASSOCIATED PROTEIN MAP2C IS A ROD-LIKE MOLECULE THAT FORMS ANTIPARALLEL DIMERS
Author(s): WILLE H; MANDELKOW EM; MANDELKOW E
Corporate Source: DESY,MAX PLANCK UNIT STRUCT MOLEC BIOL,NOTKESTR85/W-2000 HAMBURG 52//GERMANY/; DESY,MAX PLANCK UNIT STRUCT MOLEC BIOL,NOTKESTR85/W-2000 HAMBURG 52//GERMANY/
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, %%%1992%%%, V267, N15 (MAY 25), P 10737-10742
Language: ENGLISH Document Type: ARTICLE
Abstract: We have developed a procedure to isolate the microtubule-associated protein 2c (MAP2c), a juvenile form of MAP2 occurring in mammalian brain. The shape, size, self-association, and antibody interactions of MAP2c were studied. Monomeric MAP2c is an elongated molecule with a length approximately 48 nm, considerably shorter than the higher molecular weight forms MAP2a or b of adult brain. Two monoclonal antibodies whose %%%epitopes%%% are near the N or C terminus, respectively, are located close to the opposite ends of the MAP2c rods. This places constraints on the types of internal folding of the molecule.
MAP2c self-associates into dimers and fibrous aggregates. The dimers are predominantly antiparallel and nearly in register, as judged by antibody labeling.

11/7/9 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01549147 2658616
Two novel kinases phosphorylase %%%tau%%% and the KSP site of heavy neurofilament subunits in high stoichiometric ratios.
Roder, H.M.; Ingram, V.M.
Rm. 56-601, Dep. Biol., Massachusetts Inst. Technol., Cambridge, MA 02139, USA
J. NEUROSCI. vol. 11, no. 11, pp. 3325-3343 (%%%1991.%%%)
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Neurosciences Abstracts

We have identified, purified, and characterized two neurofilament/ %%%tau%%% kinases from bovine brain, PK36 and PK40, with apparent M sub(r) of 36,000 and 40,000 and with novel biochemical properties. A specially designed immunoassay for %%%phosphorylated%%% %%%epitopes%%% in neurofilament (NF) proteins was used in the early stages of the purification. Neither kinase is closely associated with the cytoskeleton. Both kinases %%%phosphorylate%%% bovine intermediate (NF-M) and heavy (NF-H) NF subunits and also bovine %%%tau%%% at the expected KSP sequences, though other sites cannot be ruled out. In human paired helical filaments, %%%tau%%%, %%%phosphorylated%%% at these same KSP sites, is a major characterized constituent. We demonstrate that both kinases can induce considerable shifts of apparent M sub(r) with SDS-PAGE for %%%tau%%% and, for the first time in vitro, also for the intermediate NF subunit.

11/7/10 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05641379 86267071 PMID: 3089107
%%%Tau%%% microheterogeneity: an immunological approach with monoclonal antibodies.
Fellous A; Ohayon R; Mazie JC; Rosa F; Luduena RF; Prasad V
Annals of the New York Academy of Sciences (UNITED STATES) %%%1986%%%, 466 p240-56, ISSN 0077-8923 Journal Code: 5NM
Contract/Grant No.: CA 26276, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The family of %%%tau%%% polypeptides purified from mammalian brain exhibit both extensive heterogeneity and large similarities in their chemical, physical, and functional properties. All the %%%tau%%% isoforms generated at a transcriptional or posttranscriptional level share the property of interacting with tubulin dimers in a specific manner. They strengthen longitudinal interactions between tubulin dimers and thus may stabilize microtubules once they are formed. Mild proteolysis or %%%phosphorylation%%% does not remove but only modulates the %%%tau%%% specific function that is probably related to the conserved sequences of the molecules. Monoclonal antibodies raised against %%%tau%%% were found to recognize %%%epitopes%%% conserved not only between species but also in different tissues. Using indirect immunofluorescence, a specific staining pattern was observed on rat neuronal cells and also on human skin fibroblasts. The same antibodies did not recognize glial cells, suggesting that these cells either do not contain detectable levels of %%%tau%%% or contain %%%tau%%% molecules different from the neuronal ones. These data suggest that %%%tau%%% protein is widely distributed, highly conserved,

and
may be preferentially associated with special subclasses of microtubules.
Record Date Created: 19860814

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Set	Items	Description
S1	15749	TAU AND ALZHEIMER?
S2	102	S1 AND PROTEIN(W)SEQUENC?
S3	74	RD S2 (unique items)
S4	19	S3 AND PY<1992
S5	10505	TAU AND PHOSPHORYLAT?
S6	1397	S5 AND PY<1993
S7	602	RD S6 (unique items)
S8	302	S7 AND ALZHEIMER?
S9	95	S7 AND EPITOPE?
S10	0	S9 NOT S7
S11	10	S9 NOT S8

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